STUDY OF CARDIOVASCULAR INVOLVEMENT IN PROTEIN ENERGY MALNUTRITION BY CLINICAL, ELECTROCARDIOGRAPHIC AND ECHOCARDIOGRAPHIC METHODS IN CHILDREN

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Certificate

This is to certify that the work entitled "**Study of Cardiovascular involvement in Protein Energy Malnutrition by Clinical, Electrocardiographic and Echocardiographic methods in Children**" has been carried out by **Dr. Gagan Agrawal** in the Department of Pediatrics, M.L.B. Medical College, Jhansi.

He has put in the necessary stay in the Department as per University regulations, and has fulfilled the conditions required for the submission of thesis according to university regulations.

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The techniques and statistical methods embodied in this thesis were undertaken by the candidate himself and the observations recorded have been checked and verified by me from time to time.

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Gagan Agrawal.

Date : 21/12/***2006*** *Gagan Agrawal*

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Introduction

INTRODUCTION

Malnutrition is defined as "a cellular imbalance between the supply of nutrients and energy, and the body's demand for them, to ensure growth and maintenance of specific functions" **(WHO)**.

Protein energy malnutrition (PEM) is the most lethal form of malnutrition affecting children and affects every 4th child worldwide **(WHO)**.

The state of world children, 2004 describes the prevalence of children who are underweight, stunted and wasted to be 47%, 46% and 16% respectively. This explains the high morbidity burden in our society.

PEM is the major health and nutritional problem in India with its high incidence in the preschool children. About 6,600 under five children die everyday of malnutrition in India. Protein energy malnutrition (PEM) accounts for death in 7% cases and is underlying cause of death in 46% cases below 5 years of age. As per recent National Family Health Survey, the most common age of PEM is between 6 months and 2 years and around 50-60% of children are malnourished by 2 years, stunting was a major problem and was observed in almost half of children.

Protein energy malnutrition (according to its severity) not only has a profound effect on external appearance of child but also has its impact on various organ systems of the body such as haematopoietic and immune system, thymolymphatic system, gastrointestinal system, musculoskeletal, cardiovascular system etc.

Cardiovascular system bears significant changes in patients with protein energy malnutrition which increases according to the severity of PEM (Singh GR et al, 1989).

Inspite of nutrition therapeutics, severely malnourished children have high mortality rate. About 50% of 10 million children's death in developing countries is contributed by PEM. The cause of death is not apparent always, even after detailed investigation and most of such death are sudden and unexpected. This instantaneous nature strongly suggests cardiac cause. (Smythe PM et al, 1962).

Earlier concept that heart is spared in malnutrition is shown to be incorrect as stated by Singh GR et al (1989) who observed various cardiovascular changes in children with severe grades of protein energy malnutrition.

Peter B et al (1989) studied the pathophysiology of involvement of heart in protein energy malnutrition and explained that cardiovascular system involvement can be due to various causes such as- (1) Myocardial atrophy secondary to inadequate protein and energy intake (2) Due to alteration of metabolic rate in PEM and thus decreasing the systemic demand for cardiac output and (3) Secondary to reduced blood volume and anaemia in children with PEM.

John G Webb et al (1986) quoted that inadequate intake of protein and energy results in proportional loss of skeletal as well as myocardial muscle. As myocardial mass decreases, it leads to decrease in cardiac contractility and the ability to generate cardiac output. However, various compensatory mechanisms comes into play, which maintains cardiac

index. This cardiac debility in turn results in poor nutrition, which viciously produce clinically significant myocardial atrophy.

Symthe et al (1962) in autopsy study of protein energy malnourished children found that the heart is underweight, looks pale or brown, flabby with slender muscle fibers and the heart walls, especially of atria were extremely thin.

Gopalan et al (1955) and Whartan et al (1962) described the histological changes in myocardial tissue in PEM such as interstitial edema and degenerative changes. Changes are most markedly observed subendocardially, especially in papillary muscles and left ventricle (Whatson et al 1969) and in conducting tissue (Smith BA et al 1962).

Brooke et al (1973) described the state of low cardiac output. He found clinical signs such as cold extremities sometimes cyanosed, decreased heart rate and poor pulse pressure in patient with severe PEM and concluded that there is an overall decrease of peripheral blood flow in severe PEM.

Smythe et al (1962) observed the radiological changes and found that heart is abnormally small which is designated as microcardia and further stated that cardiothoracic ratio which is used as an index of heart size is considerably reduced in PEM. Smythe et al (1962) recorded the electrocardiographic changes in cases of severe malnutrition such as sinus arrythmia, decrease in amplitude of P wave, QRS complex and T wave in all leads and also prolongation of QT interval, ST segment changes like concave bending and T wave change such as inversion.

Bergman et al (1978) and Hemymsfield et al (1978) studied the echocardiographic changes in protein energy malnourished children and revealed – (1) Decreased chamber size and dimension (2) Decreased left ventricular end systolic and end diastolic volume (3) Decreased contractility and cardiac output and (4) Decreased left ventricular mass.

Large amount of valuable work was done in past decades and is still going on in various parts of world to found out the effect of malnutrition on heart. Important contributions in the above field were also given by Kothari SS et al (1992), Olowanyo MT et al (1993), Phornphatkul C et al (1994), olowanyo MT et al (1995), Ocal B et al (2001), Florea VG et al (2002), Oliovares JL et al (2005) and most recent work by EL Sayed HL et al (2006) in the field of understanding heart involvement in malnutrition by using Clinical, ECG, and Echocardiographic methods. Their work had cleared the previous queries and confirmed that protein energy malnutrition has a profound effect on cardiovascular system.

The present study was undertaken to correlate the clinical radiological, electrocardigraphic and echocardiographic changes on heart in cases of severe protein energy malnutrition.

Review of Literature

REVIEW OF LITERATURE

Malnutrition has been prevalent in most parts of the world for centuries. Proctar (1926-27) first described the appearance of children without bringing nutrition into picture.

Historically **marasmus** (Greek marasmus wasting) was recognized for hundreds of years as being associated with gastroenteritis, a major contributor to high infant mortality.

Cicily Williams (1933) gave the term **'Kwashiorkar'** to tropical syndrome and mentioned that it was nutritional in origin. The term 'Kwashiorkar' has its origin from Ga language of West Africa (Kwashi-first, orkar-second) and means deposed child (Williams's 1935) i.e. the child has been displaced form mothers breast by another pregnancy or birth. It was characterized by skin changes, hair changes, edema, moonface, fatty liver, hypoalbuminemia, growth retardation and psychomotor changes. Clinical description of a disease was similar from many other countries. In West Indies e.g. the dermatosis was uncommon and edema was prominent and the term 'sugar baby' was subsequently used by Waterlow (1948) and Jellife et al (1954). Waterlow (1948) suggested that the two syndrome (marasmus and kwashiorkor) are not rigidly distinct but one could transform into another by modification in caloric intake.

Jellife (1954) coined the term **'Protein calorie malnutrition'** of early childhood to include the mild and moderate degrees and all the clinical types of the severe degrees of malnutrition. Using biochemical tests Maclaren et al (1967) was able to show that the severe degrees of PCM in

its various clinical forms of marasmus, marasmic kwashiorkor and kwashiorkor formed a spectrum of both clinical signs and changes, both being most marked in full blown kwashiorkor and pure marasmus.

FAO/WHO joint expert committee on nutrition in its 6th report proposed the broad term Protein calorie malnutrition (PCM) to embrace all such conditions as marasmus, malignant nutrition, kwashiorkor, famine edema, nutritional dystrophy etc. now the term protein calorie malnutrition has been replaced by '**Protein energy malnutrition' (PEM)** as proposed in 8th report of joint FAO/WHO expert committee (1971) on nutrition, also to emphasize this as part of overall, energy crisis of mankind the term '**Energy protein Malnutrition' (EPM)** has been used to workers to give the needed stress to energy deficit (McLaren, 1976).

Different classifications of PEM : PEM is a generalized syndrome complex and it is very difficult to classify it using a single parameter. Different classifications are given based on clinical, biochemical and anthropometric assessment.

Gomez et al (1955) is credited with the first ever classification of malnutrition using the actual weight expressed as percentage of standard weight (standard weight for age measurement used was Harvard growth standard, 50th percentile being 100%).

Gomez Classification

Weight of child	**Grades**
90-110% of standard	Normal
75-90% of standard	Ist degree malnutrition (mild)
60-74% of standard	IInd degree malnutrition (moderate)
< 60% of standard	IIIrd degree malnutrition (severe)

In later modification, Jellife (1966) included all cases with nutritional edema, irrespective of weight in 3rd degree. Its main drawback are that it assumes all children of certain age to have same weight, irrespective of their height. It also includes such children who are under weight as a result of malnutrition of the past.

Welcome Trust Classification

Weight of age (% of expected)	**Edema**	**Clinical type of PEM**
< 80	Absent	Underweight
60-80	Present	Kwashiorkor
< 60	Absent	Marasmus
< 60	Present	Marasmic kwashiorkor

* *Standard taken as 50th percentile of Harvard values.*

Waterlow and Rutishauser classification

Grade	**Stunting (height for age)**	**Wasting (weight for height)**
0	> 95%	> 90%
1	95-90%	90-80%
2	89-85%	80-70%
3	< 85%	< 70%

Waterlow mentioned that weight / height was independent.

Classification of Indian Academy of Paediatrics

Grade of malnutrition	Weight expressed as percentage of reference standards
I	71-80%
II	61-70%
III	51-60%
IV	< 50%

National sub committee of Indian academy of Paediatrics in 1972 classified PEM into 4 grades using 50^{th} percentile of Harvard growth standard as reference point.

Protein Calorie Malnutrition and Heart

In contrast to past, now with the advances in medical diagnostics, the status of cardiac function in malnutrition is better understood. Earlier concepts were that heart is spared in malnutrition have now been shown to be incorrect. Now it is agreed that in uncomplicated human and animal nutrition cardiac atrophy occurs and is in proportion to or slightly less than loss in weight.

The difficulty in diagnosing the effect of PEM on heart occurs because it rarely result in cardiac failure and also various compensatory mechanisms masks the effect of myocardial atrophy notably, blood pressure, heart rate, blood volume and metabolic demands for oxygen delivery decrease in malnourished patient.

Concepts of the effect of starvation on heart have recently changed. The earliest study by Voit in 1866 found that heart is spared in malnutrition this concept was widely accepted until it become evident from large autopsy studies of starved people that the cardiac tissue is usually reduced in proportion to the degree of emaciation of the rest of the body.

During World war II Keys and colleagues (1950) placed healthy conscientious objectors on a "European Famine diet" consisting of small quantities of turnips, potatoes and cereals. After 6 months on this low energy low protein diet, the volunteer's average weight loss was 25%, radiographs showed that the heart size was markedly decreased in all dimensions, the decrease in calculated cardiac volume being 70% of the decrease in total body weight. Since the landmark study, a decrease in heart size and myocardial atrophy have been widely documented in patients with kwashiorkor, energy restricted diets, anorexia nervosa and cardiac cachexia. Pathological studies have shown atrophy and vacuolization of cardiac muscle fibres, with a decrease in size and on occasion, fregmentation of myofibrils.

Refeeding and Cardiac Failure

Although congestive cardiac failure is rare in malnutrition, it is common during refeeding of the starved patient. Edozien and Rahim khan 1968 found that when children with protein calorie malnutrition were fed a high protein milk diet their plasma volume increased and in 20% of the children CCF developed.

Starvation is associated with a fall in heart rate, blood pressure and blood volume; however, refeeding is associated with a sudden reversal of these

compensatory factors. Further, since severe malnutrition may result in interstitial myocardial edema, cardiac compliance may decrease. The malnourished patient may not cope well with increased salt, water and energy loads. Carbohydrates and fat are potent stimuli for the release of catecholamine and activation of renin-angiotensin-aldosterone axis. This further increases blood volume and pressure. Energy intake reverses the natriuresis of the fasting state. Furthermore, catecholamines augment the shift of potassium, magnesium and phosphate into cells with potentially deleterious effect on cardiac function and rhythm.

Refeeding causes a change from the hypometabolism of starvation to hypermetabolism of refeeding. Increasing energy intake leads to corresponding increase in oxygen consumption and to meet this demand cardiac output must increase. Increased O_2 production requires increased respiratory ventilation and increased work of breathing. Heat production and heart rate progressively rise with increasing energy intake. With parental nutrition these measures of metabolism may rise above normal value. Reversal of cardiac atrophy and the ability to generate cardiac output may not keep pace with these rapidly increasing demands.

Cardiac failure is a concern in nutritionally supplemented patients even when sodium and water is kept low. It is important to begin with low energy loads in patients at risk of cardiac decompensation. It may be useful in these patients to give a higher proportion of energy as fat rather than carbohydrate. The lower respiratory quotient of fat oxidation results in less CO_2 production, thereby decreasing the work of breathing and facilitating ventilator weaning in patient with respiratory failure. The higher energy density of fat also allows that less volume to be given thus

both protein calorie malnutrition and refeeding have significant implications for the heart.

Cardiac changes in Protein Energy Malnutrtion

Morphological changes

Heymsfield and associates 1978, correlated the decrease in heart size observed radiographically with reduction in myocardial mass demonstrated by echocardiography comparing a group of malnourishd patients in hospital with height matched controls, they found by radiology a 37% decrease in heart size and by echocardiography 22% decrease in left ventricular mass due to myocardial atrophy and a 37% decrease in end diastolic volume. The decrease in heart size was proportional to the decrease in skeletal muscle bulk. Morphological change as described by (John G Webb et al, 1986) are : myocardial atrophy, myofibrilar degeneration, vacuolation of myofibrils, interstitial edema, decrease in size and fragmentation of myofibrils, mitochondrial swelling, decreased glycogen content and decreased chamber size and ventricular wall thickness.

Physiological changes

Impaired left ventricular functions, decreased contractile force, decreased cardiac output, normal or decreased stroke volume and ejection fraction and diminished diastolic compliance.

Various studies showed that there is a clinical appearance of low cardiac output in kwashiorkor. There is decreased heart rate, decreased peripheral perfusion, cold and often deeply cyanosed extremities, with a poor pulse

volume. The radial pulse may not be palpable and skin remain blanched for longer duration than usual after compression.

Radiological changes : Smythe PM et al (1962) described the radiological changes and stated that heart is abnormally small which is designated as **'microcardia'** and further stated that cardiothoracic ratio which is used as an index of heart size in considerably reduced in PEM. In his study only 7 out of 56 is falling within twice the SD of mean. C:T ratio is reduced in most cases and it was less than 0.5 (50%).

J.W. Bergman et al (1988) studied the chest radiograph of 21 patients and found that cardiothoracic ratio was below 60% in all with 14 out of 21 has CT ratio below 49% and 7 out of 21 has C:T ratio below 55%.

Electrocardiographic changes : Previously there were few reports in literature on ECG changes in malnutrition (Benedict et al, 1919; Turr, 1944; Cardazo & Egginic, 1946; Ellis, 1946; Holinger, 1948; Simonart, 1948; and Janssen and Le Roux, 1950). Keys et al (1950) also made an important contribution.

Gopalan et al (1952) studied heart rate in cases of severe malnutrition in 31 children and describe various changes. According to their study there was marked variation of heart rates before and after high protein diet. The average rise was 30% after high protein diet. On the other hand, tachycardia has been frequently reported and in that series tachycardia was present in seven cases and bradycardia in 4 cases.

Rhythm : Normal sinus rhythm was observed in 24 cases. In some patients irregular heart rate was present. All these irregularities of rhythm disappeared after treatment with high protein diet.

Interval changes : The duration of P wave and QRS complex did not show any abnormality before or after treatment, PR interval were within normal limits. The QT interval relative to cardiac cycle was increased in 15 out of 16 cases. After high protein diet there was absolute reduction in QT interval.

Amplitude changes : The most striking change observed in the ECG of malnourished children was the marked reduction in amplitude of P-wave, QRS complexes and T wave in all leads in all patients.

Echocardiographic changes : as described by Bergman J et al 1988 and Heymsfield et al (1978) in protein energy malnourished children are :

- Decreased left ventricular end systolic and end diastolic volume.
- Decreased interventricular septal wall thickness
- Decreased contractility and cardiac output.
- Decreased left ventricular mass
- Decreased diastolic performance

JW Bergman et al (1988) confirmed the presence of small heart in early stages of illness and described it due to decreased myocardial tissue. The septal thickness, left ventricular posterior wall thickness both were below 5^{th} centile lines in 74% patient whereas left ventricular chamber size were above the 5^{th} centile lines in 90% patients.

Assessment of cardiac functions : Reasons to focus on left ventricle : Most circulatory dysfunctions are due to abnormalities of left heart. Thus, clinical evaluation of cardiac function predominantly involves assessment of performance of left ventricle.

Factors controlling myocardial functions : Myocardial shortening is determined by four factors :

1) Preload
2) After load
3) Contractility
4) Heart rate and cardiac rhythm

Within physiological range, the greater the preload, the stronger the contraction and greater the extent of shortening and if greater the after load the less the amount of shortening at constant preload and after load increased contractility results in a greater extent and velocity of shortening. The final determination of cardiac function are the heart rate and rhythm. Within wide limits, with increasing rate there is enhancement of contractility. The pump performance of left ventricle depend on its ability to fill (diastolic performance) and empty (systolic performance).

Systolic performance : Left ventricular systolic performance is the ability of the left ventricle to empty. Left ventricular systolic performance can be quantified as the left ventricular ejection fraction. An operational defination of systolic dysfunction is an ejection fraction of less than 50% (Applegate RJ et al, 1990). When defined in this manner, systolic left ventricular dysfunction can result from impaired myocardial function, increased left ventricular after load and /or structural abnormalities of left heart.

Diastolic performance : Left ventricular diastolic performance is the ability of left ventricle to fill. The normal patterns of left ventricular

filling is characterized by rapid filling early in diastole, with additional filling during atrial contraction.

M-Mode Echocardiographic measurement and normal values:

Harvey Feigenbaum MD in 5th edition of Echocardiography given details about M mode echocardiography measurement and normal values.

Right ventricular dimension (RVD) : represents the distance between the trailing echoes of anterior right ventricular wall and leading echo of the right side of the interventricular septum at the R wave of the electrocardiogram.

Left ventricular internal dimension (LVID) : is measured from the trailing edge of the left side of septum to the leading edge of posterior endocardium at the R wave of electrocardiogram.

Posterior left ventricular wall thickness (PVID) : represents the distance between the leading edge of posterior left ventricular endocardium and the leading edge of epicardium at the R wave of the ECG.

Posterior left ventricular wall amplitude : Is the maximum amplitude of the posterior left ventricular subendocardial echo.

Interventricular septal wall thickness (IVS) : Is the distance between the leading edge of the left septal echo and the trailing edge of right septal echo at the R wave of the ECG.

Mid interventricular septal (Mid IVS) : Is the amplitude of the motion of left septal echo with ultrasonic beam traversing the mid portion of left ventricle.

Apical interventricular septal (apical IVS) : Is the systolic amplitude of motion of left septal echo with the ultrasonic beam directed towards the apex in the vicinity of the papillary muscles.

Left atrial dimension (LAD) : represents the distance between the trailing edge of the posterior aortic wall echo and leading edge of the posterior left atrial wall echo at the level of aortic valve at end systolic.

Normal values for children arranged by Body surface area

	BSA (M^2)	Mean (cm)	Range (cm)
RVD	0.5 or less	0.8	0.3-1.3
	0.6 to 1.0	1.0	0.4-1.8
	1.1 to 1.5	1.2	0.7-1.7
	over 1.5	1.3	0.8-1.7
LVID	0.5 or less	2.4	1.3-3.2
	0.6 to 1.0	3.4	2.4-4.2
	1.1 to 1.5	4.0	3.3-4.7
	over 1.5	4.7	4.2-5.2
LV & IV septal wall thickness	0.5 or less	0.5	0.4-0.6
	0.6 to 1.0	0.6	0.5-0.7
	1.1 to 1.5	0.7	0.6-0.8
	over 1.5	0.8	0.7-0.8
LA dimension	0.5 or less	1.7	0.7-2.4
	0.6 to 1.0	2.1	1.8-2.8
	1.1 to 1.5	2.4	2.0-3.0
	over 1.5	2.8	2.1-3.7
Aortic root	0.5 or less	1.2	0.7-1.5
	0.6 to 1.0	1.8	1.4-2.2
	1.1 to 1.5	2.2	1.7-2.7
	over 1.5	2.4	2.0-2.8
Aortic valve opening	0.5 or less	0.8	0.5-1.0
	0.6 to 1.0	1.3	0.9-1.6
	1.1 to 1.5	1.6	1.3-1.9
	over 1.5	1.8	1.5-2.0

Normal HR/PR at rest : Nelson text book,17th edition depicts the normal HR/PR as below for different age group.

Age	Lower limit of normal (per min)	Average (per min)	Upper limit of normal (per min)
Newborn	70	125	190
1-11 months	80	120	160
2 yrs	80	110	130
4 yrs	80	100	120
6 yrs	75	100	115
8 yrs	70	90	110
10 yrs	70	90	110

Normal electrocardiographic values : According to pediatric ECG by parks.

Rhythm : The normal rhythm for age is sinus rhythm, in which the sinoatrial node is the pacemaker of entire heart. There must be a P wave only one in front of each QRS complex.

P wave : The mean P wave amplitude in lead II or any other lead is about 1.5mm with a maximum of 3 mm.

QRS complexes : Handbook of circulation (Philadelphia) depicts the normal **R wave voltage (mean)** according to lead and age as follows (voltage are measured in millimeters 1mv=10mm).

Lead	6 mo-1yr	1-3 yr	3-5 yrs
V_1	13	9	7
V_2	19	16	13.5
V_5	18.5	19	20
V_6	13	12	13

and **S wave voltage (mean)** according to lead and age as follows.

Lead	6 mo-1yr	1-3 yr	3-5 yrs
V_1	8	7	13
V_2	17	21	22
V_5	3	3	2.5
V_6	2	1.2	0.7

QT interval : QT interval varies with heart rate but not with age except in infancy, therefore QT interval must be interpreted in relation to heart rate (corrected QT interval).

$$\textbf{Bazette's formula QTc} = \frac{\textbf{QT interval}}{\sqrt{\textbf{RR interval}}}$$

The QTc should not exceed 0.44 seconds except in infants. The QTc of upto 0.49 sec may be normal for first six months of age.

Mann MD (1975) studied the total body potassium and serum electrolyte concentrations in protein energy malnutrition and found that T_{BK} is almost always low and hyponatremia is common but there was no relationship between the T_{BK} and serum Na^+ and K^+ concentration and these abnormalities, particularly a very low T_{BK} appear to influence the prognosis. The expression of the observed T_{BK} as percentage of expected value for a normal child, of the same weight and height, appears to be a useful index of the severity of the total body potassium deficit.

Stephens AJ (1975) serial ECG studies were carried out on 32 cases of severe kwashiorkor and two cases of marasmus. Single reading were also carried out on 10 controls. In those cases which had a prognosis,

particularly those that died, there was a marked shift of the axis of the mean QRS vector of the limb leads to right. Those that did not deteriorate showed no such shift and those that deteriorate but eventually recovered, showed a shift to left in the recovery phase. No such shift was noted in two cases of marasmus. This suggest that this shift of mean QRS vector could be useful and generate prognostic guide.

Piassaia O et al (1980) experimental protein calorie malnutrition was produced in rats by feeding them a low protein diet for 6 weeks. Control animals were fed a high protein diet. The deficient rats showed severe restriction of body weight gain, fatty liver and hypoproteinemia. Study also demonstrated that the experimentally induced protein calorie malnutrition brings about striking pathological and electrocardiographic changes as well as increased cardiac catecholamine levels. Based on this demonstrated and considering the synchronism of morphological, electrophysiological and biochemical data, it was postulated that nutritional stress to heart raises myocardium norepinephrine concentration, and continued exposure to high level of catecholomine may play a role in the development of cardiac changes in protein energy malnutrition.

Rossi ME and Zucalato S (1982) investigated the ultrastructural features of the nutritional cardiomyopathy in protein calorie malnourished rats. PCM was induced in young rat by feeding them low protein diet (4% protein) for 6 weeks, control animals were fed a high protein diet (16% protein). The deficient rats showed severe restriction of body weight gain, fatty liver, and hypoproteinemia. The results of this study clearly demonstrated that the experimentally induced protein calorie malnutrition

brings about striking morphological changes in the heart rate of the rat. On light microscopy hyalinization and vacuolization of muscle fibres, loss of cross striations and myofibrils, small foci of necrosis, interstitial fibrosis and mononuclear cell infiltration could be detected. The ultrastructural lesions were characterized by myofibrilar degeneration, contraction band formation, dilatation of sarcoplasmic reticulam, mitochondrial swelling, dehiscence of intercalated discs and widened interstitial spaces, especially around vessels due to oedema fluid and cellular infiltration by mononuclear cells and activated fibroblasts with collagen fibres and microfibrils.

Webb JG et al (1986) quoted that heart is not spared in malnutrition and inadequate intake of protein and energy results in both proportional loss of skeletal as well as myocardial muscles. Nutritional supplementation for malnourished patients reveres the compensatory factors and may increase the short term potential for heart failure. Nutritional support play role in improving cardiac function in selected patients with rapid weight loss who are at risk for sudden death due to arrthymias. Malnutrition is also common in hospitalized patients and many patients in hospital receive nutritional supplements (parenteral/iv) this has cardiac implication as cardiac debility results in poor nutrition, which may in turn produce clinically significant myocardial atropy.

Singh GR et al (1989) evaluated 46 children between 3-48 month with varying grades of PEM for left ventricular function by echocardiography, electrocardiography, X-ray chest and clinical method. None of these children had preexisting cardiac disease, chronic illness or significant anaemia. They found children suffering uncomplicated PEM had

tachycardia, CT ratio is decreased showing decreased cardiac size. ECG changes have shown low QRS amplitude, T wave abnormality and prolonged QT_c interval. Children with grades III and IV PEM had significantly smaller cardiac chamber size and ventricular wall thickness as compared normally nourished children. Cardiac output as well as other indices of left ventricular function (percentage fractional shortening, mean rate of circumferential fibre shortening and ejection fraction) were also significantly decreased in severe PEM.

Kothari SS et al (1992) studied 25 children age 1-5 yr with severe protein energy malnutrition and compared their left ventricular mass an function to 26 healthy age and sex matched normal children and found the mean left ventricular mass in patients was lower than in the controls (25.75±9.09 gm vs 32.44±11.64 gm); $p<0.05$, CI 2.08 to 11.30). However left ventricular mass (gm/kg) body weight was signifcnatly increased in the patients (4.44 ±1.45 vs 2.42±8.07; p less than 0.001,CI 1.28 to 2.76) suggesting the relative cardiac "sparing". The systolic function indices like ejection fraction, percentage fractional shortening and velocity of circumferential fiber shortening were not significantly different in the patients and in normal children. The left ventricular end diastolic volume, stroke volume and cardiac output were reduced in proportion to decrease in body size in the patients, so the cardiac index was not reduced but slightly increased in patients. (5.95±1.91 L/min/m^2 in patients, 4.97±1.41 Lit/min/m^2 in controls; p less than 0.05, CI 0.04 to 1.92). There was no significant difference in any of these parameters of left ventricular function or mass in patients with marasmus as compared to those of patients with marasmic kwashiorkar. Among the 25 patients, however 5 patients (20%) had an ejection fraction of less than 50%. Compared to

other 20 patients these 5 patient had lower left ventricular mass (18.4±4.3 gm vs 27.5±7.8 gm) $p<0.05$ CI 1.63 to 16.75), lower left ventricular mass (gm/kg) body weight and a worse prognosis.

Olowanyo MT et al (1993) Electrocardiogram, serum electrolytes, serum albumin haematocrit and cardiotharacic ratio were recorded in 90 Nigerian children with kwashiorkor and 90 age and sex matched controls. The ECG included sinus tachycardia (91%), low QRS amplitude (100%), and prolonged QTc interval (17%). Other ECG abnormalities noted were short QTc interval (three children), prolonged PR interval (four children) and right axis deviation (two children). The mean serum sodium, potassium, calcium, albumin, hematocrit and cardiothoracic ratio were significantly lower in children with kwashiorkor than in controls ($p<0.001$). The correlation between QRS amplitude and serum potassium and calcium was poor ($P>0.05$) also, there was poor correlation between heart rate and hematocrit ($P>0.05$) and between QTc intervals and serum calcium and potassium ($P>0.05$). However, the correlation between the QRS amplitude and cardiothoracic ratio was good ($r=0.91$, $p<0.01$). These findings suggest that the ECG changes in kwashiorkor are due to myocardial atrophy.

Phornphatkul C et al (1994) studied the cardiovascular status of severely malnourished children before, during and after nutritional rehabilitation. In most children with 3rd degree malnutrition, cardiac mass was decreased on admission to the hospital and recovered subsequent to nutritional therapy. All children had echocardiographic function and doppler measurements indicative of impaired ventricular function which significantly improved during the course of hospitalization as evidenced

in part by the changes in fractional shortening ($p=0.015$), mean velocity of circumferential fibre shortening ($p=0.038$) and systolic time interval ($p=0.030$). We conclude that children with primary third degree malnutrition not only have cardiac muscle wasting, but also have inherent ventricular dysfunction as the result of severe malnutrition that responds to nutritional therapy. Particular care with fluid administration is imperative in the first week of therapy, when heart function is most compromised.

Olowanyo MT et al (1995) studied the 44 children with kwashiorkor and 44 age and sex matched controls with echocardiography (ECHO), electrocardiography and chest radiography (CXR) and found that in patients with kwashiorkar, mean values for end diastolic dimension, end systolic dimension, posterior ventricular wall thickness and shortening fraction were significantly smaller than controls, also the mean cardiothoracic ratio and QRS amplitude were significantly smaller than controls.

Etu Kudo MM 1999 studied the plasma electrolytes, total cholesterol, liver enzymes and selected antioxidant status in PEM and found that plasma total cholesterol, sodium potassium and bicarbonate, beta carotene, retinal, and uric acid were significantly lower in the malnourished group than the control group ($p<0.05$), while transaminases were significantly increased in the malnourished group ($p<0.05$) thus there is altered electrolyte and antioxidant status in protein energy malnutrition.

Ocal B et al (2001) studied the left ventricular mass (Lvmass) and systolic and diastolic functions of the left ventricle in children with PEM.

Thirty children age between 2 months 2 yr with PEM (4 kwashiorkar), seven marasmic kwashiorkor and 19 marasmus, 17 healthy age & sex matched children are studied by Doppler echocardiography and found the mean Lvmass in the patients was lower than that in controls (14.5±5.2 vs 19.8±4.7, $p < 0.05$). However the Lvmass/body surface area was not different in the patients with PEM and in the control group (52±9.2 vs 53.9±8.2 gm/m^2, $p>0.05$) indicating that Lvmass was reduced in proportion to decrease in body size in patient group (1.6±0.5 vs 2.1±0.8 L/ min, $P<0.05$) therefore cardiac index was not significantly different between the patients, and the control subjects (5.9±1.4 vs 5.7±1.6 $L/min/m^2$, $P>0.05$). Systolic function indices including ejection fraction, fractional shortening and diastolic indices were not significantly different in the groups and they thus concluded that Lvmass and cardiac output reduce in proposition to decrease in body size in patient with PEM and LV systolic and diastolic function are preserved in atrophic hearts.

Florea VG et al (2002) observed that although specific cardiac abnormality could be detected echocardiographically cachectic patients compared with patients with noncachectic chronic heart failure in a cross-sectional study, showed a significant loss of Lvmass (>20%) occurs more frequently in patients with cardiac cachexia.

Olivares JL et al (2005) studied tom compare the heart abnormalities in a group of malnourished children with control group. Thirty children with malnutrition were matched with 30 healthy children. Anthropometric, plasma level of albumin and electrolytes were determined. Among other corrected QT interval (QT_c) and QT depression (QT_d) : difference between maximum and minimum QT) were measured in 12 lead

electrocardiogram; the left ventricular mass (LVm) and left ventricular mass index (LVm) were measured by echocardiography. Regression analysis were performed with cardiac finding, as dependent variables and anthropometric and biochemical data as independent variables and found plasma level of albumin potassium and calcium were lower in malnourished children and QTd were significantly greater in patients with malnutrition than in controls (QTc 45.9±3.4 vs 400.9±17.7; p=0.000; QTd 76.4±34.1 vs 47.9±10.2 ms, p=0.000). LVm and Lvmi were significantly lower in malnourished children. [LVm, : 55.3±10.3 vs 71.4±6.9 gm, p=0.000; Lvmi 46.5±6.6 vs 60.5±4.69 g/m^2 p=0.000]

The body mass index (kg/m^2) was the most powerful predictor of the variability in QTc (39.1%), LVm (48.1%) and Lvmi (51.2%). Thus important electrocardiographic and echocardiographic abnormalities are found in malnourished children associated with their nutritional status.

EL Sayed HL et al (2006) studied the structural and functional affection of heart in protein energy malnutrition patients on admission and after nutritional recovery. The study was designed to detect the cardiac affection in PEM patients clinically, electrocardiogram, an echocardiogram are to asses the value of the cardiac marker troposin 1 in patients at risk of myocardial injury with special emphasis on the effect of nutritional rehabilitation. They carried out study on 30 PEM infants (16 non oedematous and 14 edematus) and 10 healthy age and sex matched infants, and found that electrical properties of myocardium assessed by ECG showed significant decrease in R wave and QTc interval in patients compared to controls with significant increase after nutritional rehabilitation. Parameters of left ventricular systolic function which are

ejection fraction, fractional shortening and velocity of circumferential fiber shortening were not significantly reduced in patients compared to controls.

The diastolic functions also showed no significant difference in E-wave / A wave (e/a) ratio between patients and controls. However the systolic time interval showed significantly higher LV pre-ejection index in patients in comparison to controls. Edematous and non edematous cases did not show any significant differences in ECG and ECHO data before or after nutritional rehabilitation. The hearts of two severely affected patients uniquely demonstrated marked decrease of LV end diastolic diameter (LVEDd) together with the detection of troponin I in their sera. Thus they concluded that malnutrition, regardless of its type, has a definite effect on cardiac volume, muscle mass, as well as electrical properties of the myocardium. The systolic functions of the heart are affected more than the diastolic functions and thus affection manifest only in severe cases and may constitute a bad prognostic parameters and necessitating more intense management and strict follow-up of such cases.

Aims & Objectives

AIMS AND OBJECTIVES

- To study Clinical, Electrocardiographic and Echocardiographic changes in severe protein energy malnourished children.
- To study the correlation of severe protein energy malnutrition and cardiovascular system changes.

Material & Methods

MATERIAL AND METHODS

The study was conducted in the Department of Paediatrics, Maharani Laxmi Bai Medical College, Jhansi in active collaboration with the Department of Radiology to evaluate the cardiovascular status in children with severe grades of protein energy malnutrition by Clinical, X-ray, ECG and Echocardiography.

Selection of cases : Thirty five children between 6 months to 5 years of age presenting with severe grades of protein energy malnutrition (PEM grade III & IV) were selected for the present study. Nutritional status of children was assessed on the basis of Indian Academy of Paediatrics (IAP) classification of PEM. According to this, weight for age up to 80% of reference weight (50^{th} percentile of Harvard Standard) are considered as within normal range.

Out of thirty five children taken as cases, twenty cases were of grade III malnutrition and fifteen cases were of grade IV malnutrition. Among grade III malnutrition out of 20 children, 13 were male child and 7 were female child and in grade IV malnutrition 9 were males and 6 females.

Exclusion criteria : Following groups of children were excluded from this present study.

1. Children with preexisting heart disease such as congenital heart disease, rheumatic heart disease.

2. Children with secondary malnutruition such as malnutrition due to malabsorption syndromes.

3. Children with severe anaemia (Hb<6gm%).

4. Children having severe electrolyte imbalance secondary to causes such as dehydration, renal disease and metabolic disorder (cases having serum potassium level <3meq/L were excluded).

Selection of cases

Fifteen healthy, age and sex matched children with weight ≥80% of 50th percentile of Harvard standard, and without any pre-existing illness and in which above criteria were excluded were taken as control for the present study. In control group out of fifteen children 11 were male child and 4 were females.

METHOD

A detailed history of study group with complete general and systemic examination along with all relevant investigations were done.

HISTORY

In history name, age, sex, socio-economic status of the patient was recorded in each case and a detailed history was obtained from parents and family members regarding present and past illness.

Present History : In present illness, history of any fever, loss of appetite, cough, vomiting and diarrhea, poor weight gain or weight loss, skin infections, ear discharge, convulsion, worm passage, behaviour change, pain in abdomen etc was asked.

Past History : In past illness history emphasis was given on diseases like measles, whooping cough, recurrent respiratory infections, recurrent diarrhea etc.

Family History : Family history of tuberculosis, or history of contact was also recorded in each case.

Dietary History : A detailed dietary history since birth till the inclusion in the study was recorded with emphasis on (1) upto what age exclusive breast feeding was provided (2) the age of starting of artificial milk, its quantity consumed daily, diluted or undiluted (3) the age of starting semisolid food, and its average amount consumed per day (4) and the present dietary history in form of quantity and quality of food used for feeding the child and then finally deciding from the above points whether the diet of child was adequate or inadequate.

Immunization History : Immunization status of child was recorded with special reference to BCG, DPT, OPV and measles vaccine in each case.

Milestones : The developmental history of child was recorded in all four spheres i.e gross motor, fine motor, adaptive or social and speech. The age at which child had attained different milestones was ascertained in each case and then find out whether they were normal or delayed.

Anthropometry : The following anthropometric measurements viz. weight, length or height, head circumference, chest circumference, mid arm circumference and body surface area were recorded in all cases.

CLINICAL EXAMINATION

General Examination : A thorough general examination was done in each and every case with emphasis on general appearance, hair changes, signs of vitamin A and B complex deficiency, skin changes, edema,

subcutaneous fat loss, muscle wasting, dentition, pallor, jaundice, lymphadenopathy and psychomotor changes.

Systemic Examination : In addition to general examination, systemic examination was performed to detect any systemic illness with special emphasis on cardiovascular system.

Cardiovascular System Examination : Detailed cardiovascular examination was done in each case to assess heart rate/ pulse rate, peripheral perfusion, identification of any murmur if present, finding out the sign and symptoms of congestive heart failure and sign and symptoms of shock clinically.

Respiratory System Examination : Respiratory examination was done in each case to assess signs and symptoms of respiratory infection.

Abdominal Examination : Abdominal examination was done in each case to asses hepatomegaly, splenomegaly or any other organomegaly.

Central Nervous Examination : CNS examination was done in each case to asses the behavioural /pschomotor changes such as irritability or apathy, hypotonia, delayed development/ milestones in children.

INVESTIGATIONS

Specimen Collection : Aseptic precaution was maintained while taking blood sample by veinpuncture. Blood was collected in double oxalate and plain vial before starting treatment. Investigations done were:

1) Haemoglobin
2) Serum albumin
3) Serum electrolytes (serum sodium and serum potassium)

Haemoglobin level was done to exclude severe anaemia and its effect on cardiovascular system.

Serum albumin levels done to confirm hypoproteinemia.

Serum electrolytes was done to exclude electrolyte imbalance and its effect on cardiovascular status.

Principle : Sodium was estimated by a calorimetric method based on modified Maruna and Trinders method. Sodium and proteins are precipitated together by magnesium uranyl acetate as uranyl magnesium sodium acetate. Excess of uranyl salt reacts with potassium ferrocyanide to produce a brownish colour. The intensity of the colour is inversely proportional to the sodium concentration in the specimen and is measured photometrically at 530nm.

Potassium was estimated by turbidometric method. Potassium ions in the specimen react with sodium tetra phenyl boron (boron reagent) to produce an insoluble potassium tetra phenyl boron resulting in turbid suspension. The extent of turbidity is proportional to potassium concentration and is measured photometrically at 620nm.

Normal Range

Sodium	135-155 mol/L
Potassium	3.5-5.5 mmol/L

X-ray – Chest X-ray (PA-view) was taken in all cases before refeeding to calculate the cardiothoracic ratio (C:T), which was maximum horizontal width of cardiac shadow on chest radiograph and it was used as an index of heart size. This CT ratio was then compared with controls.

Electrocardiogram : ECG with all chest and limb leads were taken and following values were calculated and compared with normal children (controls).

- Amplitude of P wave
- Amplitude of QRS complex
- ST segment changes
- T wave changes
- Any rhythm abnormality

Echocardiograpy : Echocardiography was performed in each and every case and measurements were taken according to the American Society of Echocardiographers (ASE). Following parameters in echocardiography were measured and compared with the controls.

M – Mode measurement

- Left ventricular end systolic dimension [LVID (S)]
- Left ventricular end diastolic dimension [LVID (D)]
- Interventricular septal thickness [IVS(S)]
- Interventricular septal thickness [(IVS(D)]
- Left ventricular posterior wall thickness [LVPWT (S)]
- Left ventricular posterior wall thickness [LVPWT (D)]
- Ejection fraction [EF]

Observations

OBSERVATIONS

The present study was conducted in the Department of Paediatrics, Maharani Laxmi Bai Medical College, Jhansi in active collaboration with Department of Radiology. The study comprised of two groups of cases, the first group comprised of control in which fifteen healthy children with weight for age > 80% of Harvard standard were taken.

The second group of cases comprised the study group which consisted of thirty five children of severe malnutrition (PEM Grade III and IV) according to the IAP classification.

Table -1 : Distribution of cases in study group and controls

	No. of cases (n)	Percentage
A) Study group	35	70.0
PEM Grade III	20	
PEM Grade IV	15	
B) Controls	15	30.0
Total	**50**	

Table –1 depicts the total number of cases and controls taken for the study. Above table reveals that out of total 50 children studied there were 15 controls and 35 cases of severe PEM. Out of 35 cases which were taken as study group, 20 cases belonged to PEM grade III and 15 cases were of PEM grade IV.

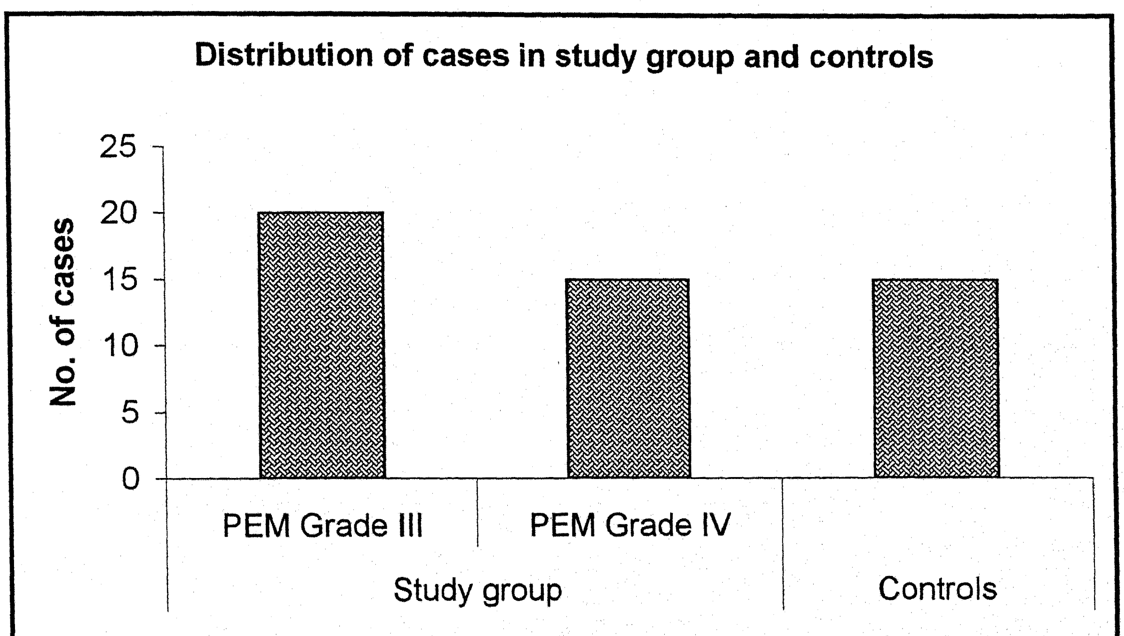

Distribution of cases in study group and controls
No. of cases
25
20
15
10
5
0
PEM Grade III
PEM Grade IV
Study group
Controls

Table-2 : Case Distribution according to sex in controls and study group

	Total no (n)	Males	Females
A) Controls	15	11	4
B) Study group	35		
PEM grade III	20	13	7
PEM grade IV	15	9	6

Table –2 describes the sex distribution in controls and study group. In control group out of 15 cases, 11 were males and 4 females, while in study group in PEM grade III, out of 20 cases 13 were males and 7 were females and among PEM grade 4 (15 cases) there were 9 males and 6 females.

Table -3 : Distribution of cases according to BSA (m^2)

	No. of cases	BSA (m^2)
A) Controls	15	≤ 0.5
B) Study group (PEM Grade III + IV)	35	≤ 0.5

Above table describes the distribution of cases according to body surface area. In controls all fifteen cases studied had BSA $\leq$ 0.5m^2. In study group all thirty five children also had BSA of $\leq$0.5m^2.

$$\textbf{BSA (m}^2\textbf{)} = \textbf{(4W+7) / (W+90)}$$

W= weight of patient in kg

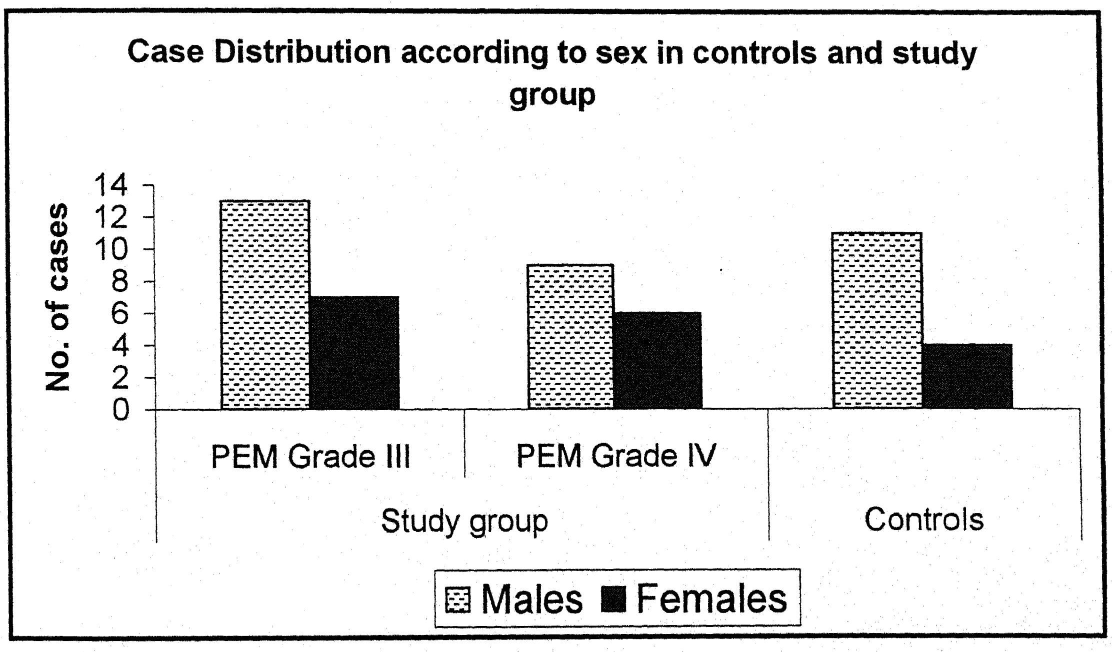

Case Distribution according to sex in controls and study group
No. of cases
14
12
10
8
6
4
2
0
PEM Grade III
PEM Grade IV
Study group
Controls
Males
Females

Table – 4 : Chief complaint : Clinical characteristics of cases in study group (n=35)

Chief complaint	No. of cases	Percentage of cases
Fever	29	82.0
Poor weight gain/weight loss	29	82.0
Loss of appetite	28	80.0
Cough	19	54.0
Diarrhoea	17	48.0
Irritability / apathy	12	34.0
Vomiting	7	20.0
Edema	7	20.0
Ear discharge	6	17.0
Skin infections	6	17.0
Adenitis	4	11.0
Convulsion	2	5.0
Pain in abdomen	2	5.0
Worm passage	1	3.0

Table –4 : depicts the presenting symptoms of cases in the study group. Fever, poor weight gain or weight loss and loss of appetite was the most common presenting complaint and was present in 82%, 82%, 80% of cases respectively, cough was present in 54% of cases, 48% of cases had diarrhoea, 34% had irritability/apathy, 20% of cases had edema and vomiting, 17% of cases had skin infections and ear discharge, 11% cases had adenitis, 5% cases had abdominal pain and convulsion and 3% cases had history suggestive of passage of worms.

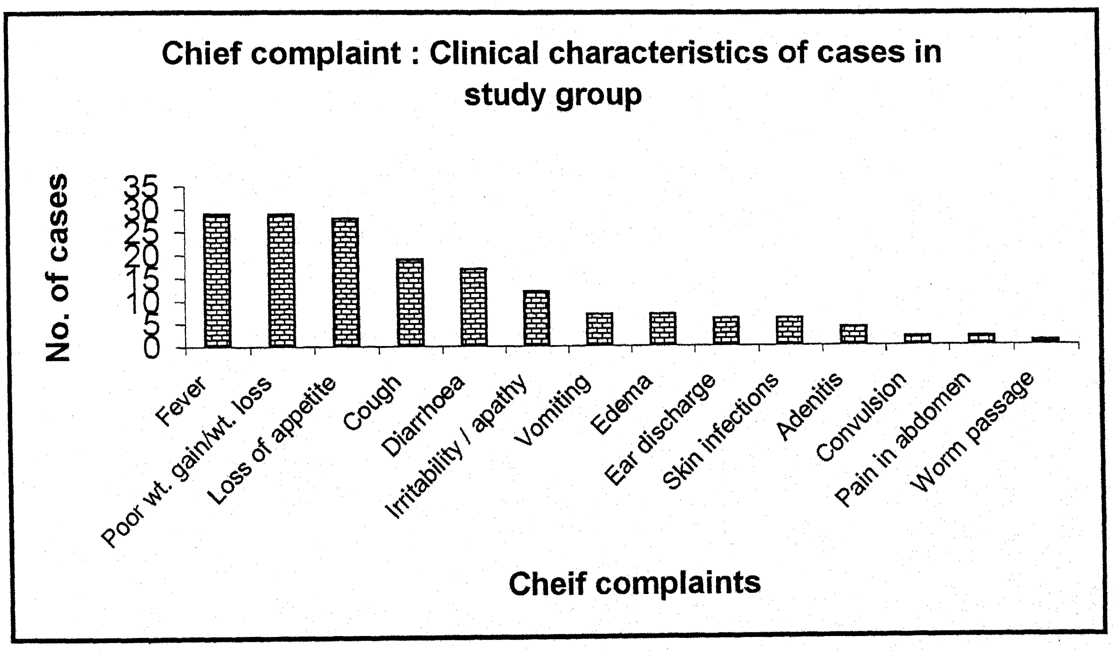

Chief complaint : Clinical characteristics of cases in study group
No. of cases
0
5
10
15
20
25
30
35
Fever
Poor wt. gain/wt. loss
Loss of appetite
Cough
Diarrhoea
Irritability / apathy
Vomiting
Edema
Ear discharge
Skin infections
Adenitis
Convulsion
Pain in abdomen
Worm passage
Cheif complaints

Table - 5 : Past history (n=35)

Diseases	No. of cases	Percentage of cases
Recurrent diarrhoea	17	48.0
Measles	13	37.0
Recurrent ARI	12	34.0
Whooping cough	2	5.0

Table – 5 shows the distribution of cases according to their past history. There was history of recurrent diarrhoea in 48% cases, 37% cases had measles in their past, 34% had a history of recurrent respiratory infection while 5% cases had a past history of whooping cough.

Table - 6 : Family history

Family history	No. of cases	Percentage of cases
History of contact with tuberculosis	10	28.0

Table – 6 shows the number of cases having history of contact with tuberculosis. There was a positive history of contact in 10 cases (28%) out of 35.

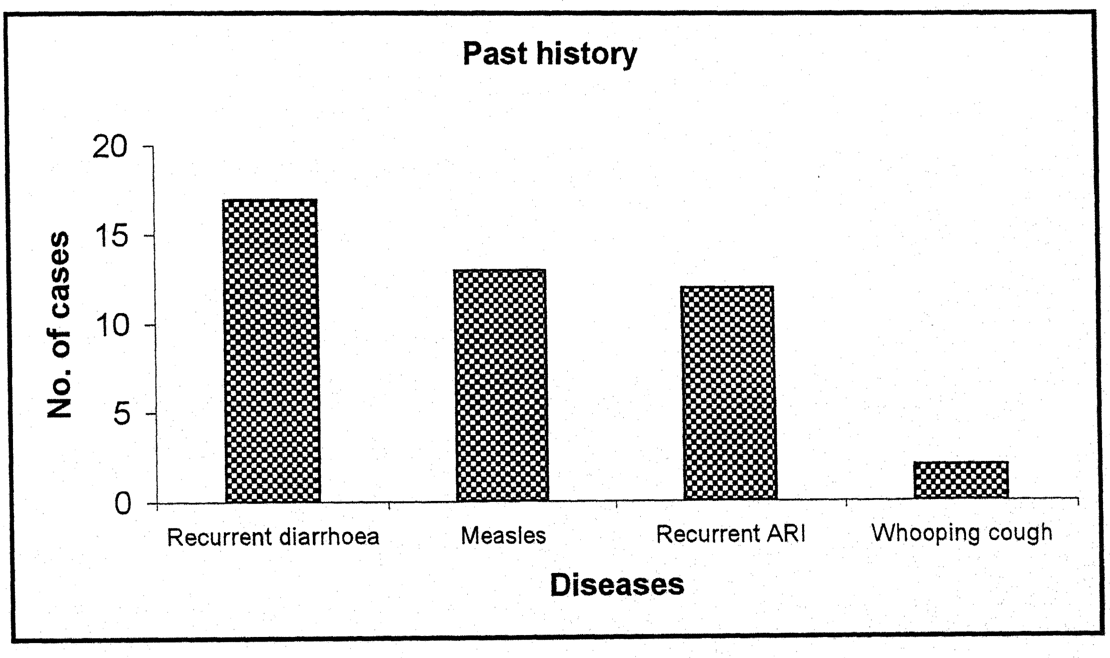

Past history
No. of cases
20
15
10
5
0
Recurrent diarrhoea
Measles
Recurrent ARI
Whooping cough
Diseases

Table - 7 : Vaccination history

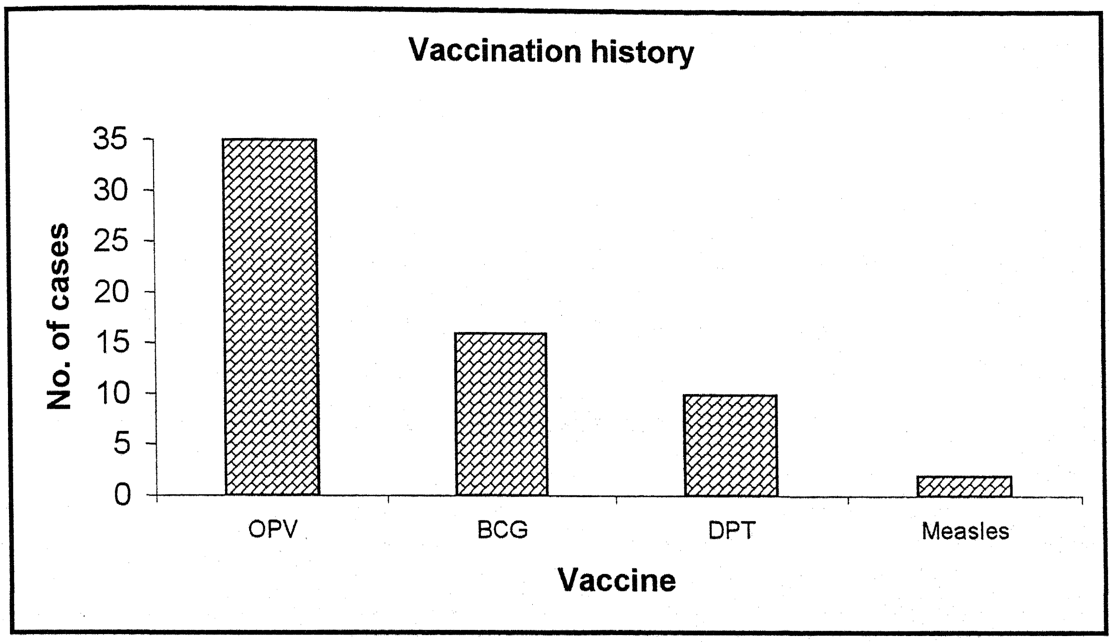
Vaccine	No. of cases	Percentage of cases
OPV	35	100.0
BCG	16	45.0
DPT	10	28.0
Measles	2	5.0

Table –7 shows the case distribution according to vaccination received. OPV was received by all 35 cases (100%), BCG scar was present in 16 cases (45%). DPT was received by 10 cases (28%) while measles vaccine was received only by 2 cases (5%)

Table - 8 : Developmental history

Mile stones	No. of cases	Percentage of cases
Normal	16	46.0
Delayed	19	54.0
PEM Grade III	5	14.0
PEM Grade IV	14	30.0

Table -8 shows the case distribution according to milestones. Milestones were normal in 16 cases (46% of total) and delayed in 19 cases (54% of total). Among 19 cases with delayed milestones 5 cases were of PEM grade III i.e. 14%, and 14 cases were of PEM grade IV i.e. 30% of total cases.


Vaccination history
No. of cases
35
30
25
20
15
10
5
0
OPV
BCG
DPT
Measles
Vaccine

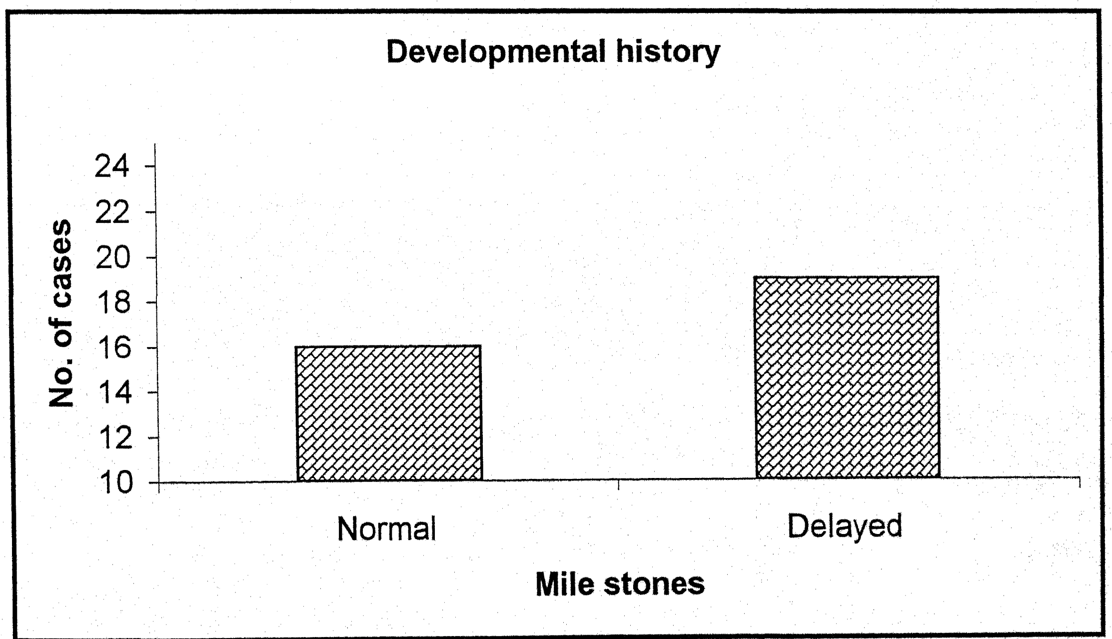

Developmental history
No. of cases
24
22
20
18
16
14
12
10
Normal
Delayed
Mile stones

Table - 9 : Socioeconomic status

Socioeconomic status	No. of cases	Percentage of cases
Low	35	100

Table – 9 shows the socioeconomic distribution, as shown in above table all the cases (100%) belonged to low socioeconomic class.

Table - 10 : Clinical Signs : General examination

Signs	No. of cases	Percentage of cases
Pallor	35	100
Subcutaneous fat loss	32	91.0
Muscle wasting	32	91.0
Hair changes	30	85.0
Signs of Vit B complex deficiency	29	82.0
Signs of Vit A deficiency	28	80.0
Adenitis	10	28.0
Edema	7	20.0

Table – 10 depicts the clinical signs in general examination in cases of study group. Pallor was most common finding present among all 35 cases (100%), 91% cases had subcutaneous fat loss and muscle wasting, 30 cases out of 35 (85%) had hair changes, signs of vit B complex deficiency and vit A deficiency were present in 29 and 28 cases respectively (i.e. 82% and 80% of total), adenitis and edema was present in 10 and 7 cases respectively out of 35 (i.e. 28% and 20% of total).

Table -11 : Anthropometry : midarm circumference

MAC	No. of cases	Percentage of cases
> 13.5 cm	Nil	0.0
12.5 –13.5 cm	Nil	0.0
< 12.5 cm	35	100

Table 11 shows the distribution of cases according to midarm circumference. Out of 35 cases, all cases i.e. 100% had a MAC < 12.5cm, thus all cases had a severe malnutrition.

Table -12 : Anthropometry : Head circumference

<table>
<tr><th>Head circumference</th><th>No. of cases</th><th>Percentage of cases</th></tr>
<tr><td>More than 3rd percentile (normal)</td><td>30</td><td>85.0</td></tr>
<tr><td>Less than 3rd percentile</td><td>5</td><td rowspan="3">15.0</td></tr>
<tr><td>PEM Grade III</td><td>2</td></tr>
<tr><td>PEM Grade IV</td><td>3</td></tr>
</table>

Table -12 shows the distribution of study group according to head circumference. From the above table, out of 35 cases in study group, 30 cases (85%) had a normal head circumference (i.e. more than 3rd percentile) while 5 cases (15%) had microcephaly (less than 3rd percentile). Among these 5 cases, 2 cases from grade III PEM and 3 cases were from grade IV PEM.

Table -13 : Systemic examination

System	Clinical findings	No.	Percentage
Respiratory system	Signs of respiratory tract infection	19	54.0
GI System	Hepatomegaly	10	28.0
	Splenomegaly	8	23.0
	Any other organomegaly	-	-
CNS	Hypotonia	24	69.0
	Irritability	7	20.0
	Apathy	5	14.0
	Convulsion	2	5.0
	Tremor	1	3.0

Table –13 shows the findings of systemic examination in cases of study group. In respiratory system examination, 19 cases (54%) had signs and symptoms of respiratory tract infection. In GI examination, hepatomegaly and splenomegaly was present in 10 and 8 cases respectively out of 35 (i.e. 28% and 23% of total). Any other organomegaly was not seen.

In CNS examination hypotonia was present in 24 cases out of 35 i.e. 69%, irritability in 7 cases (20%), apathy in 5 cases (14%), convulsions in 2 cases (5%) and tremors in 1 case (3%) out of total 35 cases in study group.

Table -14 : CVS examination : Distribution of cases according to cardiovascular findings

Clinical findings	Study group (Results)	No. of cases	%	Control	No of cases
Heart rate	Increased	24	68.0	Normal	15
Pulse volume	Decreased	2	5.0	Normal	15
Peripheral perfusion	Decreased	2	5.0	Normal	15
Cold extremities	Present	2	5.0	Normal	15

Table-14 shows the case distribution according to CVS finding. Heart rate was found to be increased in 24 cases out of 35 cases (i.e. 68% cases had tachycardia). Pulse volume was decreased in 2 cases (5%), peripheral perfusion was decreased and cold extremities present in 2 cases out of 35 i.e. 5% of total. All these clinical findings were compared with controls and we found that heart rate, pulse volume, peripheral perfusion, capillary filling time were normal in controls.

Table -15 : Haemoglobin level (gm%) in control and study group

	No. of cases	Range	Mean ± SD
A) Controls	15	8 – 12	9.9 ± 0.8
B) Study group	35	6.5 - 10.5	8.6 ± 1.2

Above table shows the haemoglobin level in controls and study group. In controls the mean Hb value was 9.9±0.8gm%, range 8-12 gm%, while in study group the mean Hb was 8.6±1.2 gm% with range from 6.5-10.5gm%.

Table -16 : Serum albumin level gm/dl in control and study group

	No. of cases	Range (gm/dl)	Mean ± SD
A) Controls	15	3.8 - 4.3	4.10 ± 0.21
B) Study group	35	2.3 – 4.1	3.0 ± 0.30
Statistical significance of S. albumin level between cases and controls			
t value	**df**	**p value**	**Significance**
2.34	48	< 0.02	Significant

Above table shows the S. albumin level in control and study group. In controls the mean serum albumin value was 4.10±0.21gm/dl, range 3.8-4.3 gm/dl, while in study group the mean value was 3.0±0.30gm/dl and range 2.3-4.1 gm/dl.

Statistics from above table shows that there was significant decrease ($p<0.02$) in serum albumin levels in severely malnourished children compared to controls.

Table -17 : Serum Na^+ level in control group and study group (meq/lit)

	No. of cases	Range	Mean ± SD
A) Controls	15	136 - 143.6	140.3 ±2.4
B) Study group	35	133 - 148.4	139.2 ± 3.5
Statistical significance of S. Na^+ value between cases and controls			
t value	**df**	**p value**	**Significance**
1.76	48	> 0.05	Not Significant

Above table shows the serum Na^+ level in controls and study group. In controls the mean S. Na^+ level was 140.3±2.4meq/lt with range being 136-143.6meq/lt, while in study group the mean level was 139.2±3.5meq/lt with range being 133-148.4 meq/lt.

Statistics from above table shows that there was no significant difference ($p>0.05$) between serum sodium levels of severely malnourished children and controls.

Table -18 : Serum K^+ level (meq/L) in control group and cases

	No. of cases	Range	Mean ± SD
A) Controls	15	3.8-4.8	4.2 ± 0.46
B) Study group	35	3-4.5	3.6 ± 0.21
Statistical significance of S. K^+ value between cases and controls			
t value	**df**	**p value**	**Significance**
2.86	48	< 0.01	Significant

Above table shows the serum K^+ level in controls and study group. In controls, the mean serum K^+ level was 4.2±0.46 meq/Lt with range from 3.8-4.8 meq/Lt. While in study group the mean level was 3.6±0.21meq/lt with range from 3-4.5 meq/Lt.

Statistics from above table shows that there was comparatively lower levels of serum potassium in severely malnourished children (study group) in comparison to controls ($p<0.01$).

Table -19 : Comparison of mean of H.R/min between study group and controls

	No. of cases	Range	Mean ± SD
A) Controls	15	90-134	106 ± 12
B) Study group	35	98-156	122 ± 16
Statistical significance of H.R. between cases and controls			
t value	**df**	**p value**	**Significance**
2.46	48	< 0.05	Significant

Above table shows the comparison of mean heart rate between study group and controls and its statistical significance. Heart rate was taken in all cases and it was compared with controls. Mean HR in study group was 122±16/min with a range from 98-156/min. In contrast, control group had a mean value of 106±12/min with a range from 90-134/min. Study group had a 13.1% more heart rate than controls.

Statistics from the above table clearly shows that there was significant increase (P<0.05) in heart rate in severely malnourished children (study group) in comparison to controls.

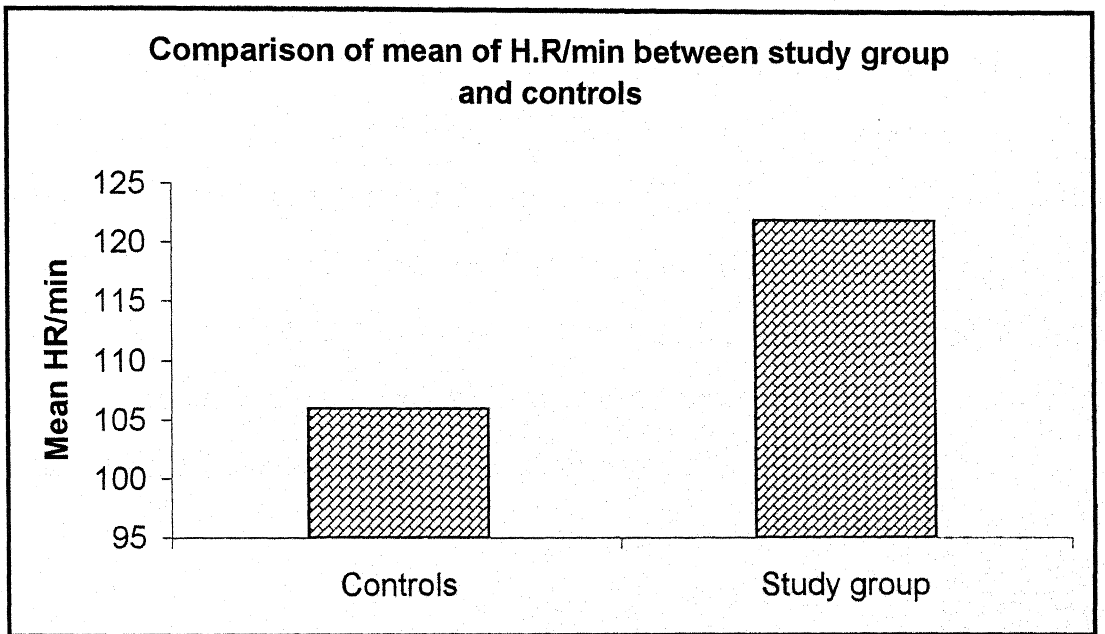

Comparison of mean of H.R/min between study group and controls
Mean HR/min
125
120
115
110
105
100
95
Controls
Study group

Table -20 : Comparison of mean CT ratio between cases and controls

	No. of cases	Range	Mean ± SD
A) Controls	15	50-56	51.6 ± 2.1
B) Study group	35	42-53	46.8 ± 1.8
Statistical significance of CT ratio between cases and controls			
t value	**df**	**p value**	**Significance**
1.418	48	< 0.001	Significant

Cardiothoracic ratio was taken in all cases in study group and controls. Cardiothoracic ratio was less than 50% in 90% cases of study group. C:T ratio in control group ranged from 50-56% with a mean of 51.6±2.1% while in study group it ranged from 42-53% with mean of 46.8±1.8%, which was 10% less than that of controls. Statistics from above table clearly shows that there was a significant decrease in C:T ratio in severely malnourished children (Study group) as compared to controls (p<0.001).

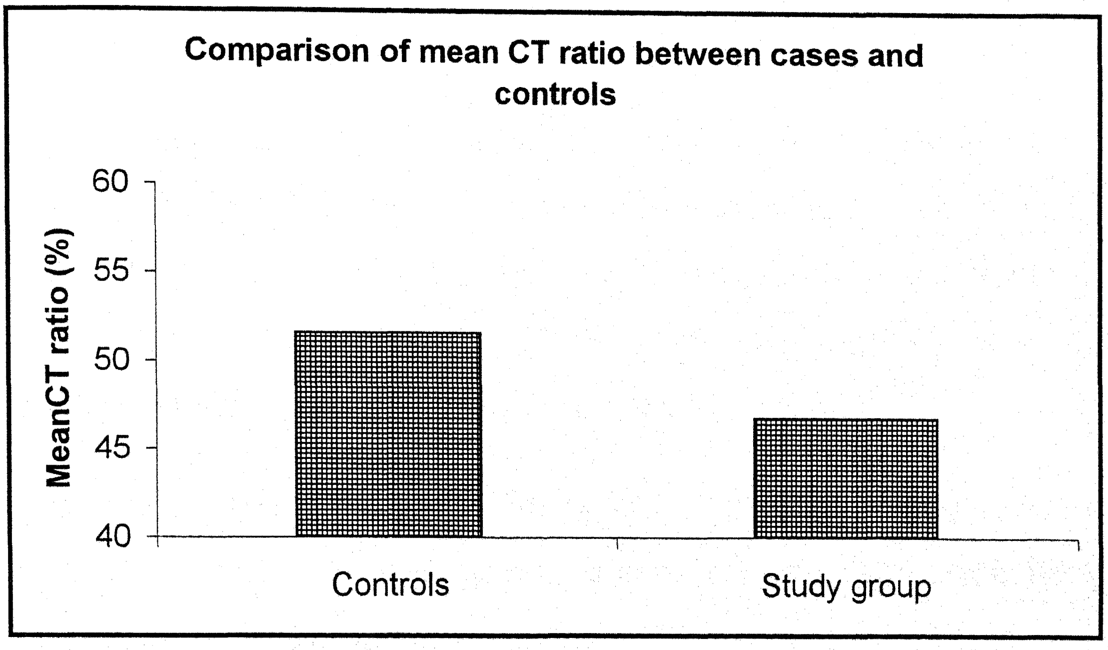

Comparison of mean CT ratio between cases and controls
MeanCT ratio (%)
60
55
50
45
40
Controls
Study group

Table -21 : Comparison of P wave amplitude (mm) between cases and controls

	No. of cases	Range	Mean ± SD
A) Controls	15	1 - 2	1.53 ± 0.12
B) Study group	35	0.5 - 1.5	1.21 ± 0.23
Statistical significance of P wave amplitude between cases and controls			
t value	**df**	**p value**	**Significance**
3.60	48	< 0.01	Significant

P wave amplitude was taken in lead II in all cases of study group and controls. P wave amplitude in control group ranged from 1-2mm with a mean of 1.53±0.12 mm while amplitude in study group ranged from 0.5-1.5mm with a mean of 1.21±0.23mm. There was a 20% decrease in amplitude in cases of study group as compared to controls.

Statistical analysis from above clearly shows that there was a significant ($p<0.01$) decrease in P wave amplitude in severely malnourished children (study group) in comparison to controls.

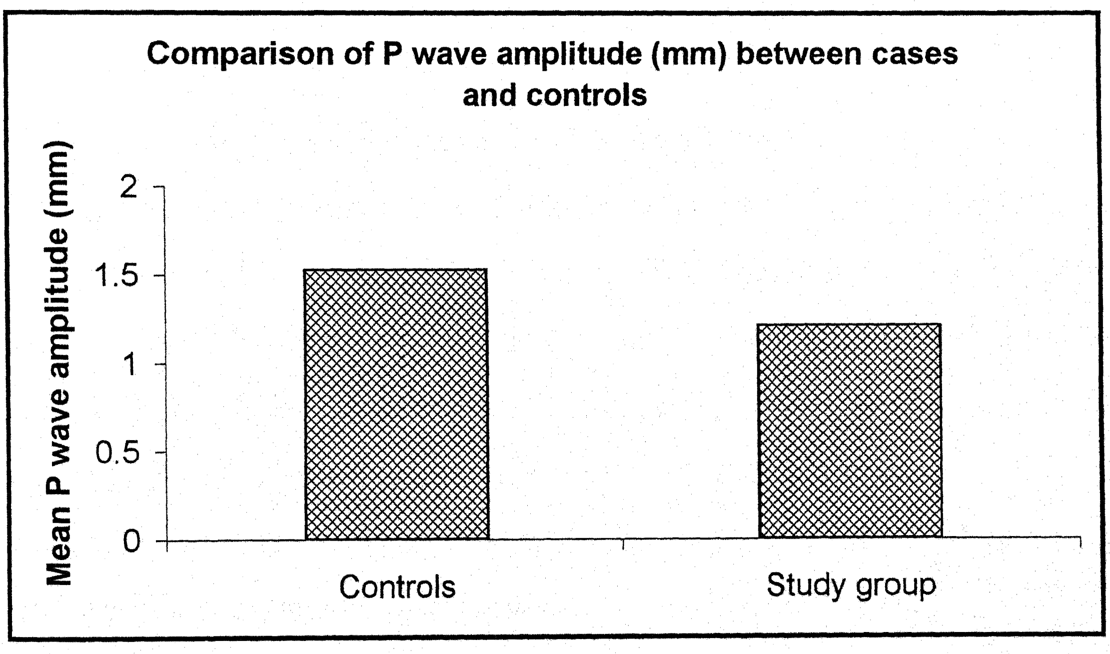
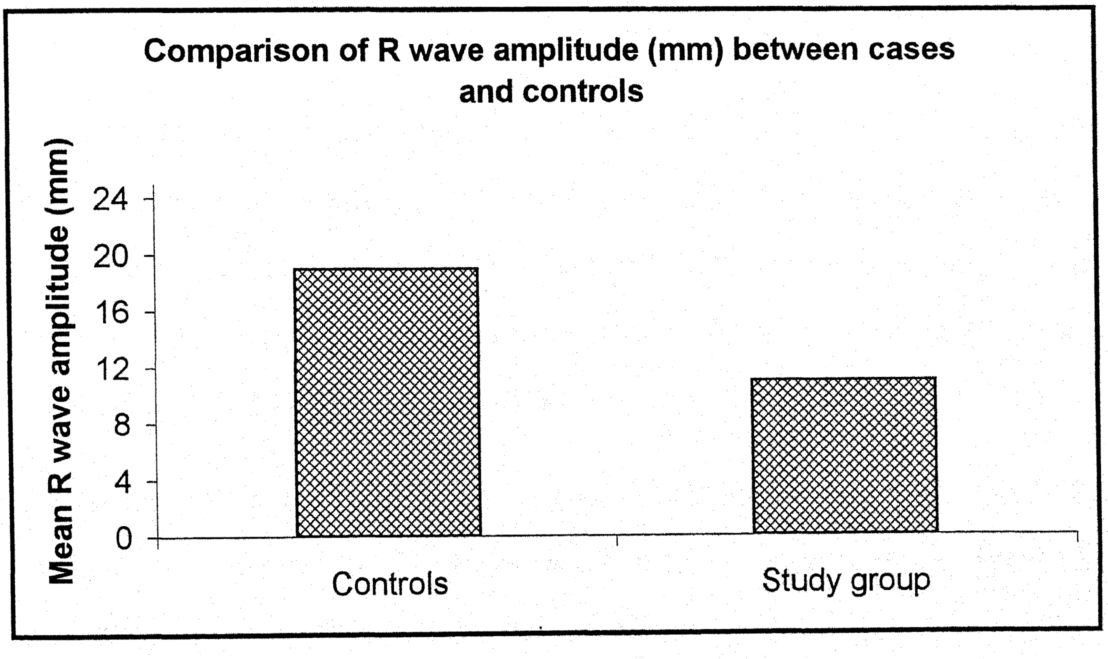

Comparison of P wave amplitude (mm) between cases and controls
Mean P wave amplitude (mm)
2
1.5
1
0.5
0
Controls
Study group

Table -22 : Comparison of R wave amplitude (mm) between cases and controls

	No. of cases	Range	Mean ± SD
A) Controls	15	15 – 24	19 ± 2.8
B) Study group	35	5 – 18	11 ± 1.9
Statistical significance of R wave amplitude in cases and controls			
t value	**df**	**p value**	**Significance**
7.48	48	< 0.001	Significant

R wave amplitude was taken in lead V_5 in all cases of study group and compared with controls. R wave amplitude in control group ranged from 15-24 mm with a mean of 19±2.8 mm while amplitude in study group ranged from 5-18mm with a mean of 11±1.9mm. There was a 40% decrease in amplitude in cases of study group than controls. Statistical analysis from above shows that there was a significant (p<0.001) decrease in R wave amplitude in study group (severely malnourished children) in comparison to controls.



Comparison of R wave amplitude (mm) between cases and controls
Mean R wave amplitude (mm)
24
20
16
12
8
4
0
Controls
Study group

Table -23 : Comparison of S wave amplitude (mm) between cases and controls

	No. of cases	Range	Mean ± SD
A) Controls	15	17 - 25	20 ± 2.9
B) Study group	35	8 - 19	12 ± 1.7
Statistical significance of S wave amplitude between cases and controls			
t value	**df**	**p value**	**Significance**
9.54	48	< 0.001	Significant

S wave amplitude was taken in lead V_2 in all cases of study group and controls. S wave amplitude in controls ranged from 17-25mm with a mean of 20±2.9mm, while in study group S wave amplitude ranged from 8-19mm with mean of 12±1.7mm. There was 42% decrease in amplitude in cases of study group than controls.

Statistical analysis from above shows that there was a significant ($p<0.001$) decrease in S wave amplitude in study group (severely malnourished children) compared to controls.

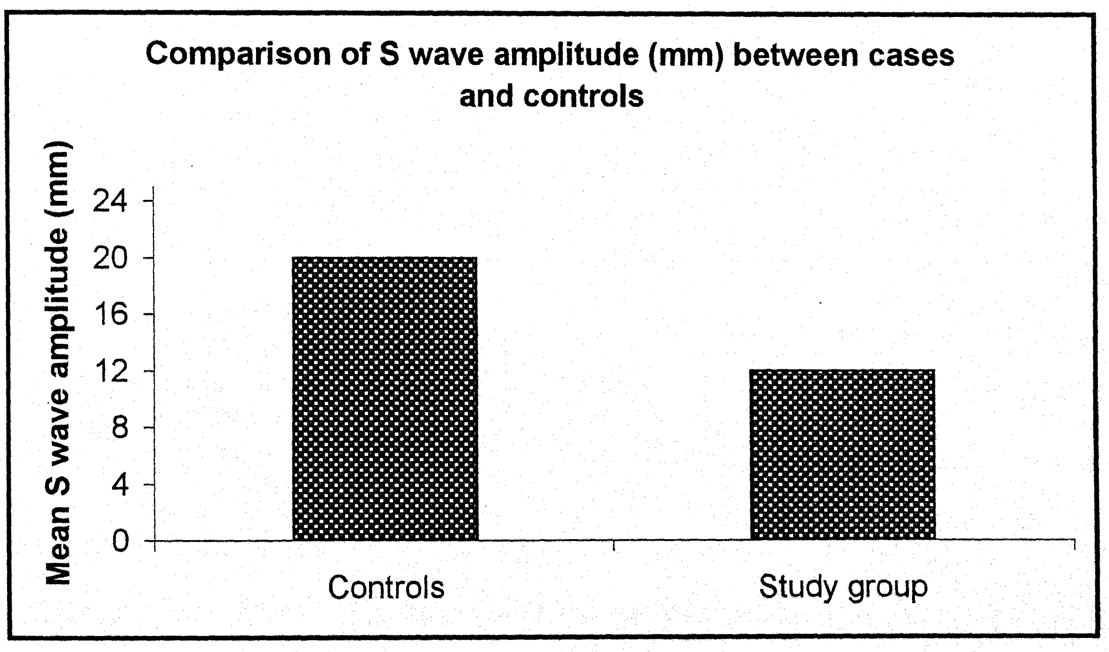

Comparison of S wave amplitude (mm) between cases and controls
Mean S wave amplitude (mm)
24
20
16
12
8
4
0
Controls
Study group

Table -24 : Comparison of echocardiographic values between study group and controls to find statistical significance according to BSA (m^2)

Variable		Study group (BSA <0.5m²)	Controls (BSA <0.5m²)	t value	p	Significance
IVS thickness (cm)	Systole	0.54±0.03	0.62±0.02	16.4	<0.001	S.
	Diastole	0.40±0.02	0.44±0.03	13.8	<0.001	S.
LVID (cm)	Systole	1.5±0.21	1.9±0.19	18.3	<0.001	S.
	Diastole	2.4±0.18	2.8±0.24	9.5	<0.001	S.
LVPWT (cm)	Systole	0.58±0.04	0.64±0.03	12.3	<0.001	S.
	Diastole	0.40±0.03	0.45±0.01	14.6	<0.001	S.
EF (%)		63.7±5.2	70±3.4	2.38	<0.05	S.

IVS - Interventricular septum thickness
LVID - Left ventricular internal dimension
LVPWT - Left ventricular posterior wall thickness
EF - Ejection fraction
BSA - Body surface area.

M mode echocardiography was done in all cases of study group and controls. Values of IVS thickness (in systole and diastole), LVID (in systole and diastole), LVPWT (in systole and diastole) and EF were taken in study group and controls with BSA <0.5mm (n=35, n=15 respectively) and then compared.

IVS thickness (systole) and IVS thickness (Diastole) in controls measured 0.62±0.02cm and 0.44±0.03cm respectively while in study group it was 0.54±0.03cm and 0.40±0.20cm respectively. There was 12.9% decrease in thickness of IVS in systole and statistical analysis showed significant decrease (p<0.001) in study group (severely malnourished) cases as compared to control cases.

LVID (systole) and LVID (diastole) was measured in both controls and study group and it came to be (1.9±0.19cm, 2.8±0.24cm) and (1.5±0.21cm, 2.4±1.8cm) respectively. There was 21% decrease in LVID in study group during systole and 14.8% decrease during diastole. Statistical analysis from above table showed that there was significant decrease in study group as compared to controls ($p<0.001$).

LVPWT (systole) and LVPWT (diastole) was also measured in both controls and study group and it came to be (0.64±0.03cm, 0.45±0.01cm) and (0.58±0.04cm, 0.40±0.03cm) respectively. There was 9% decrease in LVPWT during systole and 11% decrease during diastole. Statistical analysis from above showed significant decrease ($p<0.001$) in study group (severely malnourished) as compared to controls.

Ejection fraction was taken in all cases of study group and controls. EF in controls was 70±3.4% and in study group was 63.7±5.2%. It was 9.3% decreased in study group as compared to controls. Statistical analysis concludes the significant decrease in value of EF in study group (severely malnourished children) as compared to cases ($P<0.05$).

Discussion

DISCUSSION

Despite considerable advances in medical diagnostics in recent past, status of cardiac function in malnutrition remains unclear. After much research work, most investigators now agree that in uncomplicated human and animal undernutrition cardiac atrophy occurs, and is in proportion to or slightly less than the loss in body weight.

In the present study the main aim was to study the cardiac involvement in severe malnutrition by various methods viz clinical, X-ray, ECG and ECHO.

To serve this aim a study group was taken comprising of thirty five children of severe malnutrition (PEM grade III and IV) according to IAP classification 1972, with age group varying from 6 month to 5 years. To compare the changes fifteen healthy children of same age group and sex matched were taken as controls (table-1). Both control group and study group were further classified according to sex into male and female subgroups (table-2). To compare the values of echocardiography between severe malnutrition (study group) and control group both group were further classified according to body surface area (table-3).

Clinical characteristics : Amongst the cases of PEM we observed that the most common complaint was of fever, loss of appetite and poor weight gain/weight loss (82% of cases). Other complaints were cough in 54% cases, diarrhoea in 48% cases, irritability/apathy in 34% cases, vomiting and edema in 20% cases. 17% cases had skin infections and ear discharge, adenitis was present in 11%, convulsions and abdominal pain in 5% and worm passage in 3% cases (table no.-4).

All the symptoms found in our study group were classical symptoms with which the patient with PEM commonly presents.

While considering the past history we observed recurrent diarrhoea to be very common in malnourished children. In our study it was present in 48% cases (table no.-5). 37% children had history of measles, 34% had history of recurrent ARI and 2% had history of whooping cough. This indirectly shows the wrong feeding habits of the population and increased tendency to have repeated GIT and RTI infections in malnourished children. Similarly, high incidence of measles cases indirectly shows poor immunization coverage of the population of this area.

Family history of tuberculosis or history of contact with TB was present in 10 cases (28%) (table-6). This shows the high prevalence of disease in the population and its risk in children especially malnourished one.

Immunization status (table-7) showed that BCG was given to 16 cases (45%), OPV to all 35 cases (100%), DPT to 10 cases (28%) and measles to only 2 cases (5%). Thus we observed the poor vaccination coverage of area especially for measles vaccine.

The developmental milestones were recorded in both group of cases. It was observed that they were delayed in 19 cases (54%) among which 30% belonged to grade IV PEM (14 cases) and 14% belonged to grade III PEM (5 cases) (table-8). Thus we observed more incidence of delayed milestones in PEM grade IV compared to PEM grade III.

Dietary evaluation was done in every case and we found inadequate dietary intake, in term of calories, proteins and fats.

All cases of PEM studied belonged to low socioeconomic status, had a rural background and low literacy level (table-9).

An attempt was also made to observe the various clinical signs in all the cases. Among clinical signs studied pallor was the most common finding present in all cases (100%). Also subcutaneous fat loss and muscle wasting were common findings and present in 32 cases (91%). Hair changes were present in 30 cases (85%), signs of vit B complex deficiency and vit A deficiency were present in 29 and 28 cases (82%, 80% respectively). Adenitis was present in 10 cases (28%) and edema was present in 7 cases (20% cases) (table –10).

Anthropometry was recorded in each and every case with special reference to weight for age, mid arm circumference and head circumference. Measurement of MAC showed that all cases had MAC of <12.5cm which revealed severe malnutrition (table-11). Measurement of head circumference in study group showed that 30 cases (85%) had normal head circumference i.e. more than 3rd percentile while 5 cases (15%) had microcephaly. Among these 5 cases, 3 cases belonged to PEM grade IV and 2 belonged to grade III PEM (table –12).

A detailed systemic examination was also conducted in all the cases. In respiratory system we observed the signs and symptoms of RTI in 19 cases (54%). In GI system, hepatomegaly was present in 10 cases (28%) and splenomegaly in 8 cases (23%). In CNS examination, 24 cases showed hypotonia, which shows increase tendency of decreased tone in PEM due to muscular wasting. Psychomotor changes were present in 12 cases, irritability in 7 cases, apathy in 5 cases, convulsions were present in 2 cases while tremor in one case (table-13).

In cardiovascular findings (table-14), Heart rate showed general tendency towards sinus tachycardia. In our study 68% cases in study group had heart rate more than normal heart rate. The mean heart rate in study group was 122±16/min and in controls was 106±12/min which was significantly higher. This finding was consistent with the studies of Gopalan et al 1955, Smythe PM et al 1962, Khalil M et al 1969, Singh GR et al 1989, Olowanyo MT et al 1993. They also found tachycardia frequently in malnourished children. Khalil and Smythe reported increased heart rate in more than 90% of their cases while, Gopalan et al 1955 reported it in only 33% cases. Singh GR et al 1989 observed tachycardia in all cases. None of our cases had bradycardia, however Keys and coworkers 1950 and Smythe and Gopalan reported bradycardia in 3% and 14% in their series respectively.

Other clinical findings like decreased pulse volume, decreased peripheral perfusion, increased capillary filling time and cold extremities were found in 5% cases (2 cases out of 35). These clinical findings suggest that there is low cardiac output state in some malnourished children, while in most cases compensatory mechanisms like tachycardia, decreased activity etc. comes to play and maintains cardiac index. These findings were consistent with the findings of Smythe et al 1962, Brooke et al 1973, Alden Peter B et al 1987. Thus our study supported the fact that there is low cardiac output state present in severely malnourished children due to small heart, diminished left ventricular functions and decreased oxygen demand because of metabolic adaptation of body in malnutrition.

Haemoglobin level in the study group was found to be lower in comparison to controls. The mean haemoglobin level in study group was 8.6±1.2gm% and in controls it was 9.9±0.8gm% (table-15).

S. albumin level in study group was also found lower in comparison to controls. The mean serum albumin level in study group was 3.0±0.30 gm/dl and in controls the mean level was 4.10±0.21gm/dl (table-16). Thus there was a significant ($p<0.02$) lower values of S. albumin in severely malnourished children in comparison to controls. Phornphatkul et al (1994) found decreased mean S. albumin level in severely malnourished children, Kothari et al 1992 also found low S. albumin levels in 60% of patients.

Mean S. Sodium level in control group was 140.3±2.4meq/L and in study group the mean level was 139.2±3.5meq/l, thus there was no significant ($p>0.05$) difference between means (table-17). Singh GR et al 1989, Kothari et al 1992 also had not found any significant change in serum sodium levels in their study.

Mean serum potassium level observed in our study was lower in study group than in controls. In study group it was 3.6±0.21 meq/L while in controls it was 4.2±0.46meq/L. Thus there was significant ($p<0.01$) lower values of S. potassium in severely malnourished children as compared to controls (table-18). However, there was no such difference in the studies by Singh GR et al 1989 and Kothari et al 1992, but Phornphatkul et al 1994 found S. potassium level to be in lower range in comparison to controls in malnourished children. Mann MD et al 1975 also found that total body potassium is almost always low in severely malnourished children and hyponatremia is also common.

Cardiothoracic ratio, which is maximum transverse diameter of cardiac shadow on chest radiograph was used as an index of heart size (table-20). In our study the CT ratio was less than 50% in 90% of children in study group. The mean value in study group was 46.8±1.8%, while in controls it was 51.6±2.1%, thus there was significant ($p<0.001$) decrease in CT ratio in cases as compared to controls. Workers like Czerny et al (1914) Smythe et al (1962), Heymsfield et al (1978), Bergman et al (1988), Singh et al (1989), Olowanyo MT et al (1993), Olowanyo MT et al (1995) also found decreased cardiothoracic ratio in severely malnourished children.

Smythe et al 1962 found that, in only 7 out of 56 cases of their study, the CT ratio lied within 2 SD, rest had a significant smaller size of heart when compared to controls. Bergman et al 1988 had chest radiography of all 21 cases studied and found that cardiothoracic ratio was below 60% in all. Twenty out 21 (95%) had ratios less than 55% and 18 of 21 had values less then 49%.

Singh GR et al 1989 found mean Cardiothoracic ratio to be 46.76% in severly malnourished children and 49.12% in controls. Kothari et al 1992 in their study of 25 children, found CT ratio of less than 0.4 in 10 patients with malnutrition (40%) despite low haemoglobin levels.

Olowanyo MT et al (1993) found cardiothoracic ratio of less than 50% in 53% of their study group. They observed mean(SD) Cardiothoracic ratio of 49.39 (4.0) (range:41-63%) in patients with kwashiorkor, which was significantly lower than in the controls, whose mean (SD) ratio was 55.4 (3.5) (range 51-60%) ($p<0.0001$). Olowanyo MT et al 1995 also found decreased mean Cardiothoracic ratio (48.6±3.4%) in malnourished cases,

which were significantly smaller than controls (54±3.2%) ($p<0.001$). Hence, our findings are consisting with the findings of above workers.

Electrocardiographic changes were studied in all cases of severe malnutrition (table-19). We observed sinus tachycardia in most cases, increased heart rate was found in 68% cases of study group. The mean HR/min in study group was 122±16/min while in controls it was 106±12/min. Our observation reveals that there was a significant increase in heart rate in study group ($p<0.05$) as compared to controls. This finding is consistent with findings of Khalil et al 1969, Smythe PM et al 1962, Singh GR et al 1989, Gopalan et al 1955, Olowanyo MT et al 1993. But Keys and coworkers 1950 and Smythe et al 1962 and Gopalan et al 1955 also reported bradycardia in 3% and 14% respectively in their series.

Generalized low voltage of P wave and QRS complex were observed in malnourished children (study group) (table 21,22,23). The amplitude of P wave was decreased by 20% in study group as compared to controls. The mean amplitude of P wave in study group was 1.21±0.23mm and in controls it was 1.53±0.12mm. Thus, there was a significant decrease in P wave amplitude in severe malnutrition cases ($p<0.01$) (table –21).

Mean R wave amplitude was also 40% decreased in study group as compared to controls (table-22). The mean value was 11±1.9mm in study group while in controls it was 19±2.8mm. Thus, there was significant decrease in severe malnutrition cases ($p<0.001$).

Mean value of S wave amplitude in study group was 12±1.7mm and this value was 42% less than that of controls (mean 20±2.9mm) (table-23).

Thus, there was a significant reduction in amplitude of S wave in study group as compared to controls ($p<0.001$).

No significant changes were found in T wave and ST segment between study group and controls.

Thus electrocardiographic study which was done in all the cases was suggestive of increased heart rate, decreased amplitude of P wave and QRS complexes. There was normal rhythm and no significant changes were observed in T wave and ST segment between study group and controls. Our findings were similar to the findings observed by Gopalan et al (1955), Smythe et al (1962), Bergman JW et al (1988), Singh GR et al (1989), Olowanyo MT et al (1993), Olowanyo MT et al (1995), EL Sayed HL et al (2006). They also observed decreased amplitudes of P wave and QRS complexes in severely malnourished children.

Gopalan et al 1955 found marked reduction in amplitudes of P wave, QRS complexes in all the leads and in all cases. They observed markedly subnormal P wave and QRS complexes. They found P wave amplitude not exceeding 0.5mm in malnourished cases.

Smythe et al 1962 observed sinus tachycardia, heart rate upto 200/min, low P and QRS voltages in malnourished children. QRS voltages was below 1.5mv in 80 cases out of 91 cases studied. 49 cases had voltage less than 1mv. Bergman JW et al 1988 observed diminished amplitude in malnourished cases. They found that amplitude of R wave in V_6 was less than 25^{th} centile (as compared with age related centiles) in 18 out of 19 patients and less than 5^{th} centile in seven (37%) cases. Singh GR et al 1989 also observed low amplitude of P wave and QRS waves along with

sinus tachycardia. They observed that heart rate increases with increased severity of malnutrition. In their study, they found significant increase over 40-50% in heart rate compared to the mean control value.

Olowanyo et al 1993 observed sinus tachycardia and significant lower values of amplitude of P and QRS waves in malnourished children as compared to controls ($p<0.001$). The mean (SD) heart rate in their study group was 121 (23) beats/min was significantly higher than that of controls ($p<0.001$) where mean (SD) value was 96(16) beats/min.

Study by EL Sayed et al 2006 in malnourished children also found significant decrease in amplitudes of P waves and QRS waves as compared to controls. Hence our ECG findings are consistent with the work of above research workers.

Echocardiographic findings : M mode echocardiography was done in all cases and controls to assess the cardiac size and cardiac function in severe malnutrition. We assessed interventricular septal thickness (IVS), left ventricular internal dimensions (LVID), left ventricular posterior wall thickness (LVPWT) and ejection fraction in all cases of study group and controls and then compared them.

IVS thickness (systole) and IVS thickness (diastole) in controls measured 0.62 ± 0.02cm and 0.44 ± 0.03cm respectively, while in study group it was 0.54 ± 0.03cm, and 0.40 ± 0.02cm respectively. There was 12.9% decrease in thickness of IVS in systole and 9% decrease in diastole. Thus, there was significant decrease found ($p<0.001$) in severely malnourished children (study group).

LVID (systole and diastole) in control group came to be 1.9±0.19cm, 2.8±0.24cm and 1.5±2.1cm, 2.4±1.8cm respectively. There was 21% decrease in LVID in study group during systole and 14.8% decrease during diastole which came to be statistically significant ($p<0.001$).

LVPWT (systole and diastole) values measured as 0.64±0.03cm and 0.45±0.01cm in study group and 0.58±0.04cm and 0.40±0.03cm in controls. Here also a significant decrease was observed with 9% decrease in LVPWT during systole and 11% decrease during diastole ($p<0.001$).

Ejection fraction is the measurement of left ventricular function and it was studied in all cases and controls. A significant difference was observed in EF between cases and controls ($P<0.05$). EF in controls was 70±3.4% and in study group it was 63.7±5.2%. There was 9.3% decrease in value in study group as compared to controls.

All of the above ECHO measurements were observed to be significantly decreased in severely malnourished children than normal children. Our finding are similar to the studies of Bergman JW et al, 1988, Singh GR et al 1989, Phornphatkul et al 1994, Olowanyo MT et al 1995, Ocal B et al 2001, which was also suggestive of decreased cardiac chamber size, decreased IVS and LV posterior wall thickness and impaired LV systolic function viz EF of heart.

Bergman JW et al 1988 observed significant decreased cardiac dimensions and ventricular wall measurements in their study by M Mode echo. They observed that, 17 out of 21 patients (81%) had values below 5^{th} centile for IVS measurement and 15(71%) for LVPW thickness.

Singh GR et al 1989 also observed significantly decreased cardiac dimensions, left ventricular function viz ejection fraction in their study of severely malnourished children. The ejection fraction values were decreased upto 54.31% in severely malnourished children compared to controls.

Phornphatkul et al 1994 observed decreased septal wall thickness in 8 out of 11 children at end systole and in 3 children at end diastole LVPW thickness was observed below 5th percentile during systole in 10 children and in 9 children during diastole.

Kothari et al 1992 however did not observe any significant difference in ejection fraction ($p>0.05$). Ocal B et al 2001 also did not find any significant difference in ejection fraction ($p>0.05$), instead they found significant decrease in LV septal and posterior wall thickness and LV mass.

Recent studies by Olivares JL 2005 by Echocardiography observed significant decrease of LV mass in malnourished children (LVm 55.3 ± 10.3 vs 71.3 ± 6.9).

EL Sayed HL et al 2006 in their study observed marked decrease in cardiac dimensions in malnourished children and found that systolic function of the heart viz ejection fraction is affected more than the diastolic function but these changes manifest only in severe cases. Hence our ECHO findings corroborate with the ECHO findings of the above workers.

Summary

SUMMARY

The present study entitled "Study of cardiovascular involvement in protein energy malnutrition by clinical, electrocardiographic and echocardiographic methods in children" was conducted in Department of Pediatrics with active collaboration of the Department of Radiology, MLB Medical College, Jhansi.

- A total of fifty cases were selected for the present study, age varying from 6 months –5 years. Out of fifty cases, thirty five cases belonged to the study group and fifteen cases served as control.

- The study group cases, included those having severe malnutrition i.e. Grade III or Grade IV PEM by IAP classification 1972, while the control cases had weight for age >80% of Harvard standard. All these cases were further classified on the basis of grades of PEM, sex distribution, body surface area.

- Cases having preexisting heart disease, CHD, RHD, children with secondary malnutrition such as malabsorption syndromes, children with severe anaemia, severe electrolyte imbalance were not included in the study.

- Complete detailed history including presenting complaints, past illness, family history, dietary history, immunization history, developmental history, anthropometric measurements were recorded and a thorough general examination was done in each and every case with special emphasis on cardiovascular system.

- Blood investigations viz Hb, S. albumin, S. sodium, S. potassium was done in each and every case.

- X-ray chest was performed in all cases to calculate the cardiothoracic ratio.

- Electrocardiography and echocardiography was performed in each and every case to calculate the heart rate, P wave amplitude, QRS wave amplitude, ST and T wave changes, while ECHO was done to calculate the IVS thickness, left ventricular internal dimension, left ventricular posterior wall thickness and ejection fraction.

- All the observations were tabulated and data was analyzed statistically. The mean±SD value was calculated and statistical significance of each parameter was determined by applying Student's 't' test, thus comparing the values between study group and control group cases.

- Amongst the cases, the most common presenting complaints was fever (82%), poor weight gain/weight loss (82%) and loss of appetite (80%). The other common complaints were of cough (54%), diarrhoea (48%), irritability/apathy (34%), vomiting and edema (20%). The occurrence of other uncommon complaints like skin infections, adenitis, convulsions, pain in abdomen, worm passage varied from 17% to 3% (Table - 4).

- Past history showed recurrent diarrhoea which was commonly present in malnourished children (48%) cases. Previous history of measles and recurrent ARI was observed in 37% and 34% cases respectively (Table-5).

- There was a positive history of contact with tuberculosis in 28% cases (Table – 6).
- Vaccination status of children was incomplete except for OPV which was received by all cases (100%). BCG, DPT and measles immunization coverage was 16% and 2% respectively (Table – 7).
- Developmental history showed delayed milestones in 54% cases, out of these 30% cases belonged to PEM grade IV and 14% cases belonged to PEM grade III (Table – 8).
- Among clinical signs, pallor was the most common finding present in all cases (100%). The other common clinical signs were subcutaneous fat loss (91%), muscle wasting (91%), hair changes (85%), signs of vitamin A and B complex deficiency (82%), while adenitis and edema varied from 28-20% (Table – 10).
- Mid arm circumference was <12.5cm in all cases (100%) i.e. severe malnutrition. Head circumference measurement showed microcephaly in 15% cases, (Table 11,12) rest 85% had normal HC.
- In CNS examination most common finding was hypotonia (69%), while irritability, apathy, convulsion, tremors varied from 7% to 1%. In respiratory examination signs of RTI were present in 54% cases. In GI examination hepatomegaly (28%) and splenomegaly (23%) were frequent finding (Table-13).
- In cardiovascular system examination mean heart rate was significantly increased in malnourished children (1.22±16/min) as compared to controls (106±12/min). The other clinical findings

were low pulse volume, poor perfusion, cold extremities. These clinical changes suggests the low cardiac output state of severely malnourished children, decreased blood volume and metabolic adaptation of their body (Table – 14).

- Mean haemoglobin levels were lower in malnourished children (9.9±0.8gm/dl) as compared to controls (8.6±1.2gm/dl). There was also significant lower levels of serum albumin values in malnourished children (3.0±0.30gm/dl) as compared to controls (4.10±0.20gm/dl) ($p<0.02$) (Table – 15,16).

- Electrolyte study showed comparatively lower levels of serum potassium levels in severely malnourished children (3.6±0.21meq/lit) in respect to controls (4.2±0.46meq/lit) ($p<0.01$). Most of the values fall in normal range i.e. between 3.5-5.5meq/lit, however 9 cases (26%) had serum potassium level in range of 3-3.5meq/l. There was no significant difference observed in the mean values of serum sodium level in malnourished children as compared to controls (139.2±3.5meq/l; 140.3±2.4meq/l, $p>0.05$). Thus we observed lower haemoglobin level, decreased serum albumin level and a comparatively lower levels of serum potassium in severely malnourished children (Table – 17,18).

- Radiologic changes were suggestive of decreased heart size in malnourished children. A significant decrease in CT ratio was observed in cases as compared to controls ($p<0.001$). Over 90% of cases had CT ratio of less than 50% (Table – 20).

- Electrocardiographic changes were suggestive of increased heart rate among malnourished children as compared to controls ($p<0.05$). There was also significant decrease in amplitude of P wave and QRS complex ($p<0.001$). This decrease in amplitude can be attributed to cardiac atrophy (Table-21, 22, 23).

- M mode echocardiography findings showed significantly decreased values of IVS thickness (systole) (0.54 ± 0.03cm; 0.62 ± 0.02 cm, $p<0.001$), IVS thickness (diastole) (0.40 ± 0.02cm; 0.44 ± 0.03cm, $p<0.001$), LVID (systole) (1.5 ± 0.21cm; 1.9 ± 0.19cm, $p<0.001$), LVPWT (systole) (0.58 ± 0.04cm; 0.64 ± 0.03cm, $p<0.001$), LVPWT (diastole) (0.40 ± 0.03cm; 0.45 ± 0.01cm, $p<0.001$). The left ventricular function values viz. ejection fraction was also found to be significantly decreased as compared to controls (63.7 ± 5.2%, 70 ± 3.4%, $p<0.05$). Hence, all these findings give us the impression of cardiac atrophy and impaired left ventricular function in severe protein energy malnutrition (Table-24).

Conclusions

CONCLUSION

- From the present study we were able to conclude that children with severe grades of protein energy malnutrition had '**Cardiac atrophy**' and '**impairment of left ventricular function**', which has been documented in our study by radiological, electrocardiographic and echocardiographic methods.

- The radiological changes which suggests cardiac atrophy was decreased Cardiothoracic ratio in all cases of severe grades of malnutrition.

- The electrocardiographic findings which substantiated the presence of microcardia was evidenced by decreased P and QRS voltages.

- Similarly on echocardiographic examination the presence of decreased interventricular septal thickness, decreased left ventricular dimension, decreased left ventricular posterior wall thickness and decreased ejection fraction all suggests cardiac atrophy and impaired left ventricular function.

- Thus in nutshell we are of the view, that there is no cardiac sparing in severe grades of malnutrition as there is proportional loss of skeletal as well as cardiac muscle, as has been suggested by various other workers, who delved to study this aspect in protein energy malnutrition.

- We suggest that nutritional rehabilitation and fluid therapy of severely malnourished child should be slow, cautious and judicious, to prevent cardiac failure in these cases.

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Appendix

WORKING PROFORMA

TOPIC : STUDY OF CARDIOVASCULAR INVOLVEMENT IN PEM BY CLINICAL, ELECTROCARDIOGRAPHIC AND ECHOCARDIOGRAPHIC METHODS IN CHILDREN

Name of Guide : **Dr. R.S. Sethi (MD, D.CH)**
Name of Co-Guide : **Dr. A.K. Gupta (MD)**
Case No. :

O.P.D./M.R.D. No.	Group : Control/Study
Malnutrition with Grade :	Diagnosis :
Name :	Age/sex :
Father's Name :	Address :
Total family income : Rs.	Socio-economic status :
PRESENT ILLNESS :	
Loss of appetite Poor wt. gain/wt. Loss Fever Recurrent diarrhea Cough Recurrent URI Failure to thrive Vomiting Weight loss	Dermatosis/Skin infections Behavioural changes Adenitis Convulsion Chr. Ear discharge Worm passage Headache Pain abdomen No symptoms
PAST ILLNESS :	P.C./Pertusis/Measles/Rec. Resp. infection, Rec. Diarrhea
FAMILY HISTORY :	H/O contact : Definite/Doubtful/Nil
DIETARY HISTORY :	
Present Diet :	Calories : Proteins Adequate/ Inadequate
IMMUNIZATION HISTORY :	B.C.G. D.P.T. Polio Other
Antenatal /Natal/Post natal History :	
MILESTONES :	
Social smile Head holding Grasping of object Sits unsupported 2-3 words sentence Sphincter control Bowel	Transfer of object Standing with support Crawling Walking with support Dresses himself Holds cups Bladder
Developmental Mile Stones :	Normal/Delayed

GENERAL EXAMINATION :	
General appearance Hair Lymph nodes S/C fat loss Eyes Dentition Oedema Ant. Fontanelles Throat Rickets	Psychomotor changes Skin Face Pallor Mouth Muscle wasting Jaundice Clubbing Angular structure

ANTHROPOMETRY :	IAP classification	Waterlow Classification
Weight : Length/Height : Head Circumference : Chest Circumference : Mid-arm Circumference : Weight for Height : Height for Age :	Grade I Grade II Grade III Grade IV	Normal Stunted Wasted Wasted and stunted

ABDOMEN EXAMINATION :	Liver Spleen Any other
RESPIRATORY SYSTEM :	

CARDIOVASCULAR SYSTEM EXAMINATION :	
Heart rate : Pulse rate/Pulse volume : Blood Pressure Any murmur : Peripheral perfusion – CFT : Sign and symptoms of CHF : Sign and symptoms of shock :	

<table>
<tr><td colspan="2"><u>CENTRAL NERVOUS SYSTEM EXAMINATION</u></td></tr>
<tr><td></td><td></td></tr>
<tr><td><u>INVESTIGATIONS :</u></td><td></td></tr>
<tr><td>Haemoglobin :
Serum electrolytes – Serum Sodium :
Serum Potassium :</td><td></td></tr>
<tr><td>Serum Albumin :</td><td></td></tr>
<tr><td><u>CHEST X-RAY (PA View) :</u></td><td>Cardio thoracic ratio (C:T ratio)</td></tr>
<tr><td><u>ELECTROCARDIOGRAM :</u></td><td></td></tr>
<tr><td>Amplitude of P wave :
Amplitude of QRS complex :
ST segment changes :
T wave changes :
Any rhythm abnormality :</td><td></td></tr>
<tr><td><u>ECHO :</u></td><td></td></tr>
<tr><td colspan="2">a) Cardiac Dimensions
Left ventricular end systolic dimension [LVID (S)] :
Left ventricular end diastolic dimension [LVID (D)] :
Interventricular septal thickness [IVS(S)] :
Interventricular septal thickness [(IVS(D)] :
Left ventricular posterior wall thickness [LVPWT (S)] :
Left ventricular posterior wall thickness [LVPWT (D)] :
b) Indices of left ventricular functions
Ejection fraction [EF] :</td></tr>
</table>